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Limits: **Publication Date to 2003/11/26**

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Search	Most Recent Queries	Time	Result
#79	Search **anti p230 antibody** Limits: **Publication Date to 2003/11/26**	13:59:08	4
#78	Search **p230 antibody** Limits: **Publication Date to 2003/11/26**	13:58:04	19
#84	Search **SM5 antibody** Limits: **Publication Date to 2003/11/26**	13:55:34	9
#5	Search **FLt3 ligand and fusion protein** Limits: **Publication Date to 2003/11/26**	12:27:04	45
#42	Search **"Nakao K"[Author]** Limits: **Publication Date to 2003/11/26**	12:13:41	1530
#7	Search **FLt3 ligand and chimaera** Limits: **Publication Date to 2003/11/26**	11:16:39	28
#6	Search **FLt3 ligand and chimera** Limits: **Publication Date to 2003/11/26**	11:08:23	28
#4	Search **FLt3 ligand and fusion** Limits: **Publication Date to 2003/11/26**	11:07:25	45
#3	Search **FLt3 ligand** Limits: **Publication Date to 2003/11/26**	11:05:12	685
#2	Search **FTL3** Limits: **Publication Date to 2003/11/26**	11:04:57	0
#1	Search **FTL3 ligand** Limits: **Publication Date to 2003/11/26**	11:04:38	0

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Jun 28 2006 06:42:17

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Logon file001 29jun06 13:08:50
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***Trademarkscan - South Korea (File 655)
***Regulatory Affairs Journals (File 183)
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RESUMED UPDATING
***File 141, Reader's Guide Abstracts
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***File 516, D&B--Dun's Market Identifiers
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Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
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      Set  Items  Description
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Cost is in DialUnits
?

FILE CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE
>>>"CAPLUS" is not a valid category or service name
>>>"BIOENG" is not a valid category or service name
>>>"BIOTECHNO" is not a valid category or service name
>>>"BIOTECHDS" is not a valid category or service name
>>>"ESBIOBASE" is not a valid category or service name
>>>No valid files specified
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S 155, 159, 10, 203, 35, 5, 467, 73, 434, 34
      S1       0  155, 159, 10, 203, 35, 5, 467, 73, 434, 34
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B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34,
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       29jun06 13:10:34 User290558 Session D57.1
            $1.59    0.454 DialUnits File1
     $1.59  Estimated cost File1
     $0.53  INTERNET
     $2.12  Estimated cost this search
     $2.12  Estimated total session cost   0.454 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1950-2006/Jun 28
         (c) format only 2006 Dialog
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
 *File 159: Cancerlit is no longer updating.
Please see HELP NEWS159.
  File  10:AGRICOLA 70-2006/May
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         (c) 2006 Inst for Sci Info

      Set  Items  Description
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S (FLT3 (W) LIGAND)
           8331  FLT3
         613670  LIGAND
      S1   5254  (FLT3 (W) LIGAND)
?

S (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
          46156  CHIMERA
           1328  CHIMAERA
         514202  FUSION
        6777266  PROTEIN
          90974  FUSION(W)PROTEIN
      S2   1166  (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
?


Set     Items   Description
S1       5254   (FLT3 (W) LIGAND)
S2       1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
?

S S1 AND S2
           5254  S1
           1166  S2
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      S3        8  S1 AND S2
?

RD S3
      S4        4  RD S3  (unique items)
?

TYPE S4/FULL/1-4

  4/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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13113975   PMID: 11221836
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Enhancement of DNA vaccine potency by linkage of antigen gene to a gene encoding the extracellular domain of Fms-like tyrosine kinase 3-ligand.

Hung C F; Hsu K F; Cheng W F; Chai C Y; He L; Ling M; Wu T C
Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21287, USA.

Cancer research (United States) Feb 1 2001, 61 (3) p1080-8, ISSN 0008-5472--Print Journal Code: 2984705R
Contract/Grant No.: 5 PO1 34582-01; PHS; RO1 CA72631-01; CA; NCI; U19 CA72108-02; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Recently, Flt3 (Fms-like tyrosine kinase 3)-ligand has been identified as an important cytokine for the generation of professional antigen-presenting cells (APCs), particularly dendritic cells (DCs). A recombinant chimera of the extracellular domain of Flt3-ligand (FL) linked to a model antigen may potentially target the antigen to DCs and their precursor cells. Using human papillomavirus-16 E7 as a model antigen, we evaluated the effect of linkage to FL on the potency of antigen-specific immunity generated by naked DNA vaccines administered intradermally via gene gun. We found that vaccines containing chimeric FL-E7 fusion genes significantly increased the frequency of E7-specific CD8+ T cells relative to vaccines containing the wild-type E7 gene. In vitro studies indicated that cells transfected with FL-E7 DNA presented E7 antigen through the MHC class I pathway more efficiently than wild-type E7 DNA. Furthermore, bone marrow-derived DCs pulsed with cell lysates containing FL-E7 fusion protein presented E7 antigen through the MHC class I pathway more efficiently than DCs pulsed with cell lysates containing wild-type E7 protein. More importantly, this fusion converted a less effective vaccine into one with significant potency against established E7-expressing metastatic tumors. The FL-E7 fusion vaccine mainly targeted CD8+ T cells, and antitumor effects were completely CD4 independent. These results indicate that fusion of a gene encoding the extracellular domain of FL to an antigen gene may greatly enhance the potency of DNA vaccines via CD8-dependent pathways.

Tags: Female
Descriptors: *Cancer Vaccines--immunology--IM; *Membrane Proteins --immunology--IM; *Oncogene Proteins, Viral--immunology--IM; *Recombinant Fusion Proteins--immunology--IM; *Vaccines, DNA--immunology--IM; Animals; Antigen Presentation--immunology--IM; Antigens, Viral--genetics--GE; Antigens, Viral--immunology--IM; CD4-Positive T-Lymphocytes--immunology --IM; CD8-Positive T-Lymphocytes--immunology--IM; Cancer Vaccines--genetics --GE; Dendritic Cells--immunology--IM; Endoplasmic Reticulum--immunology --IM; Endoplasmic Reticulum--metabolism--ME; Epitopes, T-Lymphocyte

--immunology--IM; Histocompatibility Antigens Class I--immunology--IM; Humans; Immunotherapy, Active; Linkage (Genetics); Lung Neoplasms--therapy --TH; Major Histocompatibility Complex--immunology--IM; Membrane Proteins --genetics--GE; Mice; Mice, Inbred C57BL; Oncogene Proteins, Viral --genetics--GE; Protein Structure, Tertiary; Recombinant Fusion Proteins --genetics--GE; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Vaccines, DNA--genetics--GE
CAS Registry No.: 0 (Antigens, Viral); 0 (Cancer Vaccines); 0 (Epitopes, T-Lymphocyte); 0 (Histocompatibility Antigens Class I); 0 (Membrane Proteins); 0 (Oncogene Proteins, Viral); 0 (Recombinant Fusion Proteins); 0 (Vaccines, DNA); 0 (flt3 ligand protein); 0 (oncogene protein E7, human papillomavirus type 16)
Record Date Created: 20010226
Record Date Completed: 20010315

4/9/2 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013536234 BIOSIS NO.: 200200129745
The soluble Notch ligand, Jagged-1, inhibits proliferation of CD34+ macrophage progenitors
AUTHOR: Araki Hiroto (Reprint); Katayama Naoyuki (Reprint); Masuya Masahiro (Reprint); Hoshino Natsuki (Reprint); Miyashita Hiroyuki (Reprint); Sakano Seiji; Yamaguchi Motoko (Reprint); Nishii Kazuhiro (Reprint); Minami Nobuyuki; Shiku Hiroshi (Reprint)
AUTHOR ADDRESS: Second Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie, Japan**Japan
JOURNAL: Blood 98 (11 Part 1): p74a November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The Notch/Notch ligand system controls diverse cellular processes and cell fate dicisions in various organisms. The proteolytic cleavage generates transmembrane and soluble forms of Notch ligands. Although the function of transmembrane form of Notch ligands has been extensively studied, the role of their soluble form in human hematopoiesis is not well understood. As we detected the expression of Notch receptors, Notch-1 and Notch-2, on cord blood CD34+ cells as determined by flowcytometry, the activity of a soluble Notch ligand, human Jagged-1, was examined under serum-deprived conditions, using soluble human Jagged-1-IgG1 chimera protein (hJagged-1). Soluble hJagged-1 alone was not effective for colony formation by human cord blood CD34+ cells. Soluble hJagged-1 inhibited myeloid colony formation but not erythroid-mix or erythroid colony formation, in the presence of stem cell factor (SCF), IL-3, GM-CSF, G-CSF, thrombopoietin, and erythropoietin, in a dose-dependent manner. The inhibitory effects of soluble hJagged-1 on colony formation reached a minimal plateau at the concentration of 0.5 to 1 mg/ml. Cytological analysis revealed that the inhibition of myeloid colony formation by soluble hJagged-1 was mainly due to a decrease in the number of macrophage colony. Among various two-factor combinations, we found that M-CSF plus SCF, M-CSF plus IL-6, M-CSF plus flt3 ligand, and GM-CSF plus SCF predominantly supported the growth of CFU-M in our

culture system. Using these two-factor combinations, we analyzed the effects of soluble hJagged-1 on colony formation. Soluble hJagged-1 led to an inhibition of macrophage colony formation supported by M-CSF plus SCF and GM-CSF plus SCF. The inhibition of CFU-M formation was not observed when soluble hJagged-1 was added to cultures after day 2 of incubation. The suppression of CFU-M formation was not associated with a decrease in colony size. These data demonstrated that soluble hJagged-1 inhibited the growth of macrophage progenitors by acting at the early stage of macrophage development. Direct action of hJagged-1 on CD34+ cells was confirmed by the expression of Hairy Enhancer of Split-1, HES-1. These results suggest that soluble hJagged-1 may regulate human hematopoiesis in the monocyte-macrophage lineage.

REGISTRY NUMBERS: 83869-56-1: GM-CSF; 11096-26-7: erythropoietin; 9014-42-0 : thrombopoietin
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Immune System--Chemical Coordination and Homeostasis
ORGANISMS: PARTS ETC: CD34 positive cell--blood and lymphatics, immune system; CD34 positive macrophage progenitor--blood and lymphatics, immune system, proliferation, regulation; cord blood--blood and lymphatics; macrophage--blood and lymphatics, immune system, development; myeloid cell--blood and lymphatics, immune system
CHEMICALS & BIOCHEMICALS: CFU-M; GM-CSF {granulocyte-macrophage colony stimulating factor}; Hairy Enhancer of Split-1--expression; IL-3 {interleukin-3}; IL-6 {interleukin-6}; Jagged-1--soluble notch ligand; Jagged-1-IgG1 chimera protein--fusion protein; M-CSF; Notch receptor; Notch-1; Notch-2; erythropoietin; flt3 ligand; stem cell factor; thrombopoietin
MISCELLANEOUS TERMS: hematopoiesis; myeloid colony formation; Meeting Abstract; Meeting Poster; Meeting Abstract; Meeting Poster
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
10064 Biochemistry studies - Proteins, peptides and amino acids
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
17002 Endocrine - General
25502 Development and Embryology - General and descriptive
34502 Immunology - General and methods

4/9/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07889422 Genuine Article#: 220TN Number of References: 40
Title: The soluble interleukin-6 (IL-6) receptor/IL-6 fusion protein enhances in vitro maintenance and proliferation of human CD34(+)CD38(-/low) cells capable of repopulating severe combined immunodeficiency mice
Author(s): Kollet O; Aviram R; Chebath J; benHur H; Nagler A; Shultz L; Revel M; Lapidot T (REPRINT)
Corporate Source: WEIZMANN INST SCI,PAULINE RECANATI CAREER DEV CHAIR IMMUNOL, DEPT IMMUNOL/IL-76100 REHOVOT//ISRAEL/ (REPRINT); WEIZMANN INST SCI,PAULINE RECANATI CAREER DEV CHAIR IMMUNOL, DEPT IMMUNOL/IL-76100 REHOVOT//ISRAEL/; WEIZMANN INST SCI,DEPT MOL GENET/IL-76100 REHOVOT//ISRAEL/; KAPLAN HOSP,DEPT OBSTET & GYNECOL/IL-76100 REHOVOT//ISRAEL/; HADASSAH UNIV HOSP,DEPT BONE MARROW TRANSPLANT/IL-91120 JERUSALEM//ISRAEL/; JACKSON LAB,/BAR

HARBOR//ME/04609
Journal: BLOOD, 1999, V94, N3 (AUG 1), P923-931
ISSN: 0006-4971 Publication date: 19990801
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: ARTICLE
Geographic Location: ISRAEL; USA
Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: HEMATOLOGY
Abstract: In vitro maintenance and proliferation of human hematopoietic stem cells is crucial for many clinical applications. Early hematopoietic cells express low levels of FLT-3 and c-kit receptors, as well as the interleukin-6 (IL-6) receptor signal transducing element, gp130, but do not express IL-6 receptor itself. Therefore, we have attempted to maintain human cord blood or bone marrow CD34(+) cells ex vivo in serum-free cultures containing stem cell factor (SCF) and FLT-3 ligand (FL) alone or together with a new recombinant molecule of soluble IL-6 receptor fused to IL-6 (IL6RIL6 chimera). The effect of IL6RIL6 chimera on the proliferation and differentiation of CD34(+) cells was compared with that of each chimera component added separately, The engraftment potential of in vitro-cultured cells was determined using our recently established functional in vivo assay for primitive human severe combined immunodeficiency (SCID)-repopulating cells (SRC), We report here that IL6RIL6 chimera induced significantly higher levels of progenitors and SRC compared with SCF + FL alone or together with IL-6 and soluble IL-6 receptor. IL6RIL6 chimera prolonged in vitro maintenance of SRC for up to 14 days. Stimulation of CD34(+)CD38(-/low) enriched cells with IL6RIL6 chimera maintained the early CD34(+)CD38(-/low) cell subpopulation, which could be detected in vitro for up to 14 days. Moreover, IL6RIL6 chimera preferentially stimulated the growth of early CD34(+)38(-/low) cells, resulting in significantly higher levels of progenitors compared with more mature CD34(+)38(+) cells. Taken together, these findings demonstrate the importance of IL6RIL6 chimera in stimulating the proliferation of early CD34(+) CD38(-)gp130(+)IL-6R(-) cells in vitro and extended maintenance of progenitors and SRC, (C) 1999 by The American Society of Hematology.
Identifiers--KeyWord Plus(R): HUMAN HEMATOPOIETIC-CELLS; BONE-MARROW STROMA; HUMAN CORD-BLOOD; C-KIT LIGAND; IN-VITRO; PROGENITOR CELLS; FLT3 LIGAND; STEM-CELLS; CYTOKINE; GP130
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PAONESSA G, 1995, V14, P1942, EMBO J
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SHIMIZU Y, 1998, V91, P3688, BLOOD
SUI X, 1995, V92, P2859, P NATL ACAD SCI USA
TAGA T, 1989, V58, P573, CELL
TAJIMA S, 1996, V184, P1357, J EXP MED
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ZANJANI ED, 1994, V20, P331, BLOOD CELLS

4/9/4 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06403692 Genuine Article#: YQ652 Number of References: 31
Title: Interleukin-6 receptor-interleukin-6 fusion proteins with enhanced interleukin-6 type pleiotropic activities
Author(s): Chebath J; Fischer D; Kumar A; Oh JW; Kolett O; Lapidot T; Fischer M; RoseJohn S; Nagler A; Slavin S; Revel M (REPRINT)
Corporate Source: WEIZMANN INST SCI,DEPT MOL GENET/IL-76100 REHOVOT//ISRAEL/ (REPRINT); WEIZMANN INST SCI,DEPT MOL GENET/IL-76100 REHOVOT//ISRAEL/; INTERPHARM LABS,/IL-76110 NESS ZIONA//ISRAEL/; WEIZMANN INST SCI,DEPT IMMUNOL/IL-76100 REHOVOT//ISRAEL/; UNIV MAINZ,DEPT MED, SECT PATHOPHYSIOL/D-55101 MAINZ//GERMANY/; HADASSA MED CTR,BONE MARROW TRANSPLANTAT CTR/IL-91120 JERUSALEM//ISRAEL/
Journal: EUROPEAN CYTOKINE NETWORK, 1997, V8, N4 (DEC), P359-365
ISSN: 1148-5493 Publication date: 19971200
Publisher: JOHN LIBBEY EUROTEXT LTD, 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE
Language: English Document Type: ARTICLE
Geographic Location: ISRAEL; GERMANY
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: IMMUNOLOGY; BIOCHEMISTRY & MOLECULAR BIOLOGY; CELL BIOLOGY
Abstract: An sIL-6R/IL-6 chimera, directly fusing the natural forms of soluble IL-6 receptor and IL-6, as found in human body fluids, was produced in transfected human cells, The secreted p85 glycoprotein was active at a concentration of 120 pM to produce growth-arrest and spindleoid differentiation of murine melanoma F10.9 cells, which do not respond to IL-6 alone. This fusion protein was as active as the yeast-produced p56 fusion protein containing a shortened sIL-6R, linked through a flexible peptide chain to IL-6 (Hyper IL-6), The concentration of Hyper IL-6 needed to arrest the growth of F10.9 cells was much lower than that needed of a combination of IL-6 and sIL-6R, added separately, Hyper IL-6 was also more active than IL-6 in stimulating growth of murine plasmacytoma T1165 cells, the half maximal stimulation being obtained at 2 pM Hyper IL-6 versus 23 pM for IL-6. In

order to evaluate the effect of the fused sIL-6R/IL-6 proteins on human hematopoietic primitive progenitor cells, they were added to suspension cultures of CD34(+) cells from human cord blood in addition to both flt3/flk2 ligand (FL) and stem cell factor (SCF). Fused sIL-6R/IL-6 produced a marked stimulation of cell expansion and a marked increase in the number of colony forming units when subsequently plated in semi-solid medium with IL-3, GM-CSF, SCF and erythropoietin. Ex-vivo maintenance and expansion of early progenitor cells in bone marrow transplantation protocols may be a potential application for the sIL-6R/IL-6 chimeric glycoproteins.

Descriptors--Author Keywords: growth inhibition ; melanoma ; hematopoiesis ; interleukin-6

Identifiers--KeyWord Plus(R): HUMAN-BREAST-CARCINOMA; CELLS IN-VITRO; PROGENITOR CELLS; FLT3 LIGAND; IL-6 RECEPTOR; GROWTH; CYTOKINE; AFFINITY; GP130; INTERFERON-BETA-2

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SHAH AJ, 1996, V87, P3563, BLOOD
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TAGA T, 1989, V58, P373, CELL
TAJIMA S, 1996, V184, P1357, J EXP MED
VEIBY OP, 1996, V157, P2953, J IMMUNOL
WARD LD, 1994, V269, P23286, J BIOL CHEM
YAMASAKI K, 1988, V241, P825, SCIENCE
ZILBERSTEIN A, 1986, V5, P2529, EMBO J

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Set	Items	Description
S1	5254	(FLT3 (W) LIGAND)
S2	1166	(CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3	8	S1 AND S2
S4	4	RD S3 (unique items)

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S (S1 AND CHIMERA)

5254	S1
46156	CHIMERA

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      S5       80  (S1 AND CHIMERA)
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RD S5
      S6       52  RD S5  (unique items)
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Set      Items   Description
S1        5254   (FLT3 (W) LIGAND)
S2        1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3           8   S1 AND S2
S4           4   RD S3  (unique items)
S5          80   (S1 AND CHIMERA)
S6          52   RD S5  (unique items)
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S (APOPTOSIS AND ANTIBODY)
          544452  APOPTOSIS
         1758699  ANTIBODY
      S7   39485  (APOPTOSIS AND ANTIBODY)
?


Set      Items   Description
S1        5254   (FLT3 (W) LIGAND)
S2        1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3           8   S1 AND S2
S4           4   RD S3  (unique items)
S5          80   (S1 AND CHIMERA)
S6          52   RD S5  (unique items)
S7       39485   (APOPTOSIS AND ANTIBODY)
?

S S7 AND S6
           39485  S7
              52  S6
      S8       1  S7 AND S6
?

TYPE S8/FULL/1

  8/9/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2006 Elsevier Science B.V. All rts. reserv.

11614988     EMBASE No: 2002181249
  Stromal cell-derived factor 1/CXCR4 signaling is critical for early human
 T-cell development
  Hernandez-Lopez C.; Varas A.; Sacedon R.; Jimenez E.; Mun(tilde)oz J.J.;
Zapata A.G.; Vicente A.
  A. Vicente, Departamento de Biologia Celular, Facultad de Biologia,
  Universidad Complutense, 28040 Madrid  Spain
  AUTHOR EMAIL: avicente@bio.ucm.es
  Blood ( BLOOD ) (United States)   15 JAN 2002, 99/2 (546-554)
  CODEN: BLOOA   ISSN: 0006-4971
  DOCUMENT TYPE: Journal ; Article
  LANGUAGE: ENGLISH   SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 42
```

The present study investigated the potential role of stromal cell-derived factor 1 (SDF-1) in human intrathymic T-cell differentiation. Results show that SDF-1 is produced by human thymic epithelial cells from the subcapsular and medullary areas, and its receptor, CXCR4, is upregulated on CD34SUP+ precursor cells committed to the T-cell lineage. Chimeric human-mouse fetal thymus organ culture (FTOC) seeded with purified CD34SUP+ thymic progenitors and treated with neutralizing antibodies against SDF-1 or CXCR4 showed a significant reduction of the number of human thymocytes and an arrested thymocyte differentiation in the transition between CD34SUP+ precursor cells and CD4SUP+ immature thymocytes. SDF-1-treated FTOC showed an increase of human thymocyte numbers, mainly affecting the most immature subpopulations. Moreover, these results suggest that CXCR4/SDF-1 signaling is not critical for the CD34SUP+ cell precursor recruitment to the thymus. On the other hand, SDF-1 significantly increased the viability of CD34SUP+ T-cell precursors modulating the expression of BCL-2 and BAX genes, and stimulated the proliferation of CD34SUP+ thymic precursor cells, particularly in synergy with interleukin 7 (IL-7), but not with other cytokines, such as stem cell factor or flt3-ligand. Accordingly, only IL-7 was able to up-regulate CXCR4 expression on CD34SUP+ thymic progenitors. In addition, deprivation of SDF-1 partially inhibited human thymocyte expansion induced by IL-7 in human-mouse FTOC. This study indicates that SDF-1/CXCR4 signaling is required for the survival, expansion, and subsequent differentiation of human early thymocytes and identifies a new mechanism by which IL-7 mediates its effects on human thymopoiesis. (c) 2002 by The American Society of Hematology.

DRUG DESCRIPTORS:
*stromal cell derived factor 1--endogenous compound--ec; *chemokine receptor CXCR4--endogenous compound--ec
CD34 antigen--endogenous compound--ec; neutralizing antibody; CD4 antigen --endogenous compound--ec; protein bcl 2--endogenous compound--ec; protein Bax--endogenous compound--ec; interleukin 7--endogenous compound--ec; stem cell factor--endogenous compound--ec; Flt3 ligand--endogenous compound--ec
MEDICAL DESCRIPTORS:
*T lymphocyte
thymocyte; epithelium cell; lymphocyte differentiation; organ culture; prolymphocyte; cell survival; apoptosis; phenotype; chimera; cell proliferation; human; nonhuman; mouse; controlled study; human cell; animal tissue; embryo; fetus; infant; preschool child; article; priority journal
CAS REGISTRY NO.: 188900-71-2 (chemokine receptor CXCR4); 219306-68-0 (protein bcl 2); 171404-15-2 (Flt3 ligand)
SECTION HEADINGS:
  021 Developmental Biology and Teratology
  026 Immunology, Serology and Transplantation
?

Set	Items	Description
S1	5254	(FLT3 (W) LIGAND)
S2	1166	(CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3	8	S1 AND S2
S4	4	RD S3 (unique items)
S5	80	(S1 AND CHIMERA)
S6	52	RD S5 (unique items)
S7	39485	(APOPTOSIS AND ANTIBODY)
S8	1	S7 AND S6

?

S (S1 AND (FUSION (W) PROTEIN))
5254 S1

```
          514202  FUSION
         6777266  PROTEIN
           90974  FUSION(W)PROTEIN
      S9     121  (S1 AND (FUSION (W) PROTEIN))
?

RD S9
     S10      60  RD S9  (unique items)
?

S (S10 AND APOPTOSIS)
              60  S10
          544452  APOPTOSIS
     S11      11  (S10 AND APOPTOSIS)
?

RD S11
     S12      11  RD S11  (unique items)
?

TYPE S12/FULL/1-11

  12/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14868444   PMID: 15120328
 Induction of potent TRAIL-mediated tumoricidal activity by
 hFLEX/Furin/TRAIL recombinant DNA construct.
  Wu Xiaofeng; Hui Kam M
  Gene Vector Laboratory, Division of Cellular and Molecular Research,
National Cancer Center, 11 Hospital Drive, Singapore 169610, Singapore.
  Molecular therapy - the journal of the American Society of Gene Therapy (
United States)  May 2004,  9  (5)  p674-81,  ISSN 1525-0016--Print
Journal Code: 100890581
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Subfile:  INDEX MEDICUS
  Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has been
shown to exert selectively cytotoxic activity against many tumor cells but
not normal cells. On the other hand, the ligand for the receptor tyrosine
kinase Fms-like tyrosine kinase 3 (Flt3L) is a growth factor for
hematopoietic progenitors and is a potent stimulating factor for dendritic
and NK cells. Previously, we have demonstrated that it is possible to
inhibit the outgrowth of primary tumors by the administration of an hFlex
(the extracellular domain of the Flt3L) and TRAIL (amino acid residues
95-281) secreted fusion protein. Here, we report that by the insertion of a
linker sequence encoding the cleavage site for the Golgi-expressed
endoprotease furin between the DNA sequences encoding hFlex and TRAIL, the
tumoricidal activity of the cleaved TRAIL protein generated was greatly
enhanced in comparison to the hFlex/TRAIL fusion protein. Furthermore, we
demonstrate that intratumoral injection of the hFlex/furin/TRAIL DNA, in
conjunction with cationic liposomes, significantly suppressed the outgrowth
of the human CNE-2 nasopharyngeal tumor xenografts in SCID mice. In situ
histological examinations confirmed the expression of TRAIL in the treated
tumor nodules and the induction of apoptosis was also evidenced by the
presence of numerous pyknotic nuclei.
```

Descriptors: *Furin--genetics--GE; *Membrane Glycoproteins--genetics--GE; *Membrane Proteins--genetics--GE; *Neoplasms--therapy--TH; *Tumor Necrosis Factor-alpha--genetics--GE; Animals; Annexin A5--analysis--AN; Antibodies --immunology--IM; Apoptosis; Apoptosis Regulatory Proteins; Carcinoma --pathology--PA; Carcinoma--therapy--TH; Cell Line, Tumor; DNA, Recombinant--genetics--GE; DNA, Recombinant--therapeutic use--TU; Dendritic Cells--immunology--IM; Furin--therapeutic use--TU; Humans; Immunochemistry; Liposomes--therapeutic use--TU; Membrane Proteins --therapeutic use--TU; Mice; Mice, SCID; Nasopharyngeal Neoplasms --pathology--PA; Nasopharyngeal Neoplasms--therapy--TH; Neoplasm Transplantation; Plasmids--genetics--GE; Plasmids--therapeutic use--TU; Propidium--analysis--AN; Recombinant Fusion Proteins--genetics--GE; Recombinant Fusion Proteins--therapeutic use--TU; Research Support, Non-U.S. Gov't; Transfection; Transplantation, Heterotopic; Xenograft Model Antitumor Assays

CAS Registry No.: 0 (Annexin A5); 0 (Antibodies); 0 (Apoptosis Regulatory Proteins); 0 (DNA, Recombinant); 0 (Liposomes); 0 (Membrane Glycoproteins); 0 (Membrane Proteins); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 0 (TNF-related apoptosis-inducing ligand); 0 (Tumor Necrosis Factor-alpha); 0 (flt3 ligand protein); 36015-30-2 (Propidium)

Enzyme No.: EC 3.4.21.75 (Furin)

Record Date Created: 20040503

Record Date Completed: 20041217

12/9/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14000070 PMID: 12417909

Increasing bioactivity of Flt3 ligand by fusing two identical soluble domains.

Lu Chang-Ming; Yu Jian-Feng; Huang Wei-Da; Zhou Xuan; Zhang Wei-Yan; Xi Hong; Zhang Xue-Guang

Biotechnology Research Institute, Soochow University, Suzhou 215007, China.

Sheng wu hua xue yu sheng wu wu li xue bao Acta biochimica et biophysica Sinica (China) Nov 2002, 34 (6) p697-702, ISSN 0582-9879--Print

Journal Code: 20730160R

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Flt3 ligand (FL) is a hematopoietic growth factor, initiating its in tracellular signaling cascade by binding to counterpart receptor and driving receptor dimerization. The native form of soluble FL in vivo is mainly monomeric. In this study, we constructed a rFL-FL fusion protein cDNA by linking two copies of cDNA encoding the soluble domain of FL in tandem and expressed it in Pichia pastoris. On SDS-polyacrylamide gel electrophoresis, the rFL-FL fusion protein showed a molecular weight of 43 kD, agreeing well with the predicted value. The 43 kD protein was further confirmed by Western blot using polyclonal rabbit anti-human FL antibody. The rFL-FL fusion protein exhibited about 10-fold increment in its activity on colony formation of bone marrow progenitor cells. RFL-FL fusion protein also exerted more potent effect than monomeric FL on extending the survival of starving Raji cells.

Descriptors: *Membrane Proteins--pharmacology--PD; Animals; Apoptosis --drug effects--DE; Binding Sites--genetics--GE; Bone Marrow Cells

--cytology--CY; Bone Marrow Cells--drug effects--DE; Cell Count; Cell Division--drug effects--DE; Cell Survival--drug effects--DE; Dose-Response Relationship, Drug; Humans; Membrane Proteins--genetics--GE; Mice; Recombinant Proteins--genetics--GE; Recombinant Proteins--pharmacology--PD ; Research Support, Non-U.S. Gov't; Tumor Cells, Cultured
CAS Registry No.: 0 (Membrane Proteins); 0 (Recombinant Proteins); 0 (flt3 ligand protein)
Record Date Created: 20021105
Record Date Completed: 20030303

12/9/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13444940 PMID: 11685115
Costimulation blockade promotes the apoptotic death of graft-infiltrating T cells and prolongs survival of hepatic allografts from FLT3L-treated donors.
Li W; Lu L; Wang Z; Wang L; Fung J J; Thomson A W; Qian S
Thomas E. Starzl Transplantation Institute and Department of Surgery, University of Pittsburgh Medical Center, E1540 Biomedical Science Tower, 200 Lothrop Street, Pittsburgh, Pennsylvania, 15213, USA.
Transplantation (United States) Oct 27 2001, 72 (8) p1423-32, ISSN 0041-1337--Print Journal Code: 0132144
Contract/Grant No.: DK 29961; DK; NIDDK; DK 49745; DK; NIDDK
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
BACKGROUND: Mouse liver grafts are accepted across major histocompatibility complex (MHC) barriers and induce donor-specific tolerance without immunosuppressive therapy. By contrast, hepatic allografts from donors treated with the hematopoietic growth factor fms-like tyrosine kinase 3 ligand (FL), which dramatically increases hepatic interstitial dendritic cells (DC), are rejected acutely (median survival time 5 days). This switch from tolerance to rejection is associated with a marked reduction in apoptotic activity of graft-infiltrating T cells. We hypothesized that T-cell costimulation, provided by markedly enhanced numbers of donor antigen presenting cells (APCs), might inhibit apoptosis, promote expansion of T helper 1 cells and play a key role in acute liver rejection. METHODS: C3H (H2k) recipients of orthotopic liver grafts from FL-treated B10 (H2b) donors were given cytotoxic T-lymphocyte antigen 4: immunoglobulin (CTLA4Ig), a chimeric fusion protein that blocks the B7-CD28 costimulatory pathway, or control human immunoglobulin (200 microg) on the day of transplantation (day 0). Livers and spleens were removed on day 4. Cryostat sections were stained for interleukin (IL)-12 or by terminal deoxynucleotidyl transferase-mediated dUTP-nick end labeling (TUNEL). Expression of mRNA encoding interferon (IFN)-gamma and IL-10 was determined by RNase protection assay. Suspensions of graft-infiltrating cells (GICs) and spleen cells were analyzed for apoptotic (TUNEL+) T-cell subsets by flow cytometry. CTL activity of GICs and circulating alloantibody levels were determined by cytotoxicity assays. RESULTS: Survival of liver grafts from FL donors was markedly prolonged by CTLA4Ig administration. This effect was associated with reductions in IFN-gamma and IL-10 gene transcripts within the GIC population, and with decreases in donor-specific CTL and NK cell activities and circulating anti-donor alloantibody levels. At the same

time, there were marked increases in TUNEL+ CD4+ and especially CD8+ cells, both within the grafts and in the spleens of CTLA4Ig-treated mice. CONCLUSIONS: Signaling via the B7-CD28 pathway appears to play a key role in the switch from tolerance to rejection that is precipitated by markedly enhanced numbers of donor DCs. Inhibition of acute liver allograft rejection by CTLA4Ig, linked to restoration of apoptotic activity of graft-infiltrating T cells, further suggests that deletion of these cells may be critical for promotion of long-term allograft survival.

Tags: Male

Descriptors: *Antigens, CD28--physiology--PH; *Antigens, CD80--physiology --PH; *Apoptosis; *Graft Survival; *Immunoconjugates; *Membrane Proteins --pharmacology--PD; *T-Lymphocytes--physiology--PH; Animals; Antigens, Differentiation--pharmacology--PD; Cytokines--biosynthesis--BI; Isoantibodies--biosynthesis--BI; Liver Transplantation; Lymphocyte Activation; Mice; Mice, Inbred Strains; Research Support, U.S. Gov't, P.H.S.; Transplantation, Homologous

CAS Registry No.: 0 (Antigens, CD28); 0 (Antigens, CD80); 0 (Antigens, Differentiation); 0 (Cytokines); 0 (Immunoconjugates); 0 (Isoantibodies); 0 (Membrane Proteins); 0 (cytotoxic T lymphocyte-associated antigen 4-immunoglobulin); 0 (cytotoxic T-lymphocyte antigen 4); 0 (flt3 ligand protein)

Record Date Created: 20011030

Record Date Completed: 20011204

12/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13155379 PMID: 11273779

Regression of human mammary adenocarcinoma by systemic administration of a recombinant gene encoding the hFlex-TRAIL fusion protein.

Wu X; He Y; Falo L D; Hui K M; Huang L

Center for Pharmacogenetics, University of Pittsburgh, Pittsburgh, Pennsylvania 15261, USA.

Molecular therapy - the journal of the American Society of Gene Therapy (United States) Mar 2001, 3 (3) p368-74, ISSN 1525-0016--Print

Journal Code: 100890581

Contract/Grant No.: AI43916; AI; NIAID; CA 74918; CA; NCI; CA73743; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

The tumor necrosis factor (TNF)-related apoptosis-inducing ligand, TRAIL, is a new member of the TNF family. It can specifically induce apoptosis in a variety of human tumors. To investigate the possibility of employing the TRAIL gene for systemic cancer therapy, we constructed a recombinant gene encoding the soluble form of the human Flt3L gene (hFlex) at the 5' end and the human TRAIL gene at the 3' end. Such design allows the TRAIL gene product to be secreted into the body circulation. We have also demonstrated that the addition of an isoleucine zipper to the N-terminal of TRAIL greatly enhanced the trimerization of the fusion protein and dramatically increased its anti-tumor activity. The fusion protein reached the level of 16-38 microg/ml in the serum after a single administration of the recombinant gene by hydrodynamic-based gene delivery in mice. A high level of the fusion protein correlated with the regression of a human breast tumor established in SCID mice. No apparent toxicity was observed in the

SCID mouse model. In addition, the fusion protein caused an expansion of the dendritic cell population in the C57BL/6 recipient mice, indicating that the hFlex component of the fusion protein was functional. Thus, the hFlex-TRAIL fusion protein may provide a novel approach, with the possible involvement of dendritic cell-mediated anti-cancer immunity, for the treatment of TRAIL-sensitive tumors.

Descriptors: *Adenocarcinoma--therapy--TH; *Gene Therapy; *Mammary Neoplasms, Experimental--therapy--TH; *Membrane Glycoproteins--genetics--GE ; *Membrane Proteins--genetics--GE; *Tumor Necrosis Factor-alpha--genetics --GE; Adenocarcinoma--genetics--GE; Adenocarcinoma--immunology--IM; Animals; Apoptosis--drug effects--DE; Apoptosis Regulatory Proteins; Cytotoxicity, Immunologic--genetics--GE; Cytotoxicity, Immunologic --immunology--IM; Dose-Response Relationship, Drug; Gene Expression Regulation, Neoplastic; Gene Transfer Techniques; Humans; Mammary Neoplasms, Experimental--genetics--GE; Mammary Neoplasms, Experimental --immunology--IM; Membrane Glycoproteins--secretion--SE; Membrane Glycoproteins--therapeutic use--TU; Membrane Proteins--secretion--SE; Membrane Proteins--therapeutic use--TU; Mice; Mice, SCID; Recombinant Fusion Proteins--biosynthesis--BI; Recombinant Fusion Proteins--blood--BL; Recombinant Fusion Proteins--therapeutic use--TU; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Tumor Cells, Cultured ; Tumor Necrosis Factor-alpha--secretion--SE; Tumor Necrosis Factor-alpha --therapeutic use--TU

CAS Registry No.: 0 (Apoptosis Regulatory Proteins); 0 (Membrane Glycoproteins); 0 (Membrane Proteins); 0 (Recombinant Fusion Proteins); 0 (TNF-related apoptosis-inducing ligand); 0 (Tumor Necrosis Factor-alpha); 0 (flt3 ligand protein)

Record Date Created: 20010329

Record Date Completed: 20010802

12/9/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11475429 PMID: 9305592

New understanding of the pathogenesis of CML: a prototype of early neoplasia.

Clarkson B D; Strife A; Wisniewski D; Lambek C; Carpino N

Sloan-Kettering Institute for Cancer Research, Memorial Hospital for Cancer and Allied Diseases, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.

Leukemia - official journal of the Leukemia Society of America, Leukemia Research Fund, U.K (ENGLAND) Sep 1997, 11 (9) p1404-28, ISSN 0887-6924--Print Journal Code: 8704895

Contract/Grant No.: CA08748; CA; NCI; CA64593; CA; NCI

Publishing Model Print; Comment in Leukemia. 1998 Feb;12(2) 136-8; Comment in PMID 9519773; Comment in Leukemia. 1998 Mar;12(3):444-5; Comment in PMID 9529143; Comment in Leukemia. 1998 Mar;12(3):446-7; Comment in PMID 9529144

Document type: Case Reports; Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The 9;22 chromosomal translocation characteristic of CML results in a fused bcr/abl gene and an abnormal fusion protein, p210bcr/abl. Relative to normal c-abl, p210bc1/abl has elevated tyrosine kinase activity that is essential for its transforming activity. We recently reported a prominent 62 kDa GAP-associated P-tyr protein and five additional consistent but less

prominent P-tyr proteins as well as five more minor P-tyr proteins that are constitutively tyrosine phosphorylated in primary primitive lineage negative (lin-) chronic phase CML blasts but not in comparable primary lin- normal blasts. The GAP-associated p62 protein has now been purified, sequenced and its gene has been cloned; it is a previously unidentified protein and is currently being characterized. In analyzing P-tyr proteins in primary lin- normal blasts in response to various hematopoietic cytokines, we found a striking similarity in the tyrosine phosphorylation of four major and three minor proteins after stimulation with c-kit ligand (KL) and the P-tyr proteins that are constitutively phosphorylated in primary primitive lin- chronic phase CML blasts. Other cytokines tested (ie GM-CSF, G-CSF, IL-3, FLT3 ligand, TPO, EPO) were much less active or stimulated phosphorylation of other proteins. KL/c-kit and bcr/abl have some similar activities including enhancing survival and expansion of hematopoietic progenitor cells, probably acting primarily on early progenitors at the time of lineage commitment rather than on self-renewing stem cells. Activation of growth factor receptors promote a cascade of protein phosphorylations that can ultimately result in a wide range of cellular responses. Sustained activation of discrete signaling pathways in some types of cells results in differentiation, whereas transient activation instead causes a proliferative response; in other cell types, the converse is true. It may be postulated that stem cells and primitive progenitors are at a particularly susceptible stage of development that renders them especially responsive to sustained bcr/abl-induced phorphorylation of a number of signaling proteins that are components of critical regulatory pathways, including c-kit. The affected pathways control and coordinate multiple diverse cell processes including proliferation, differentiation, maturation and apoptosis, processes that are normally tightly regulated and integrated. Perturbation of these key pathways in primitive progenitors would be expected to seriously disrupt orderly hematopoiesis and could also explain the multiple subtle pleiotropic biological abnormalities characteristically observed in later maturing CML compartments that we have collectively designated 'discordant maturation'. The true situation is undoubtedly very complex and involves interaction of multiple cytokines and signaling pathways that we are now trying to define. Constitutive downstream activation of critical pathways in susceptible early progenitors that normally require KL or other factors for activation could explain most if not all features of the disease. (179 Refs.)

Tags: Female; Male

Descriptors: *Fusion Proteins, bcr-abl--physiology--PH; *Leukemia, Myeloid, Philadelphia-Positive--pathology--PA; Adolescent; Adult; Apoptosis ; Bone Marrow--pathology--PA; Cell Division; Cell Separation; Cell Survival ; Hematopoiesis; Humans; Leukemia, Myeloid, Philadelphia-Positive--genetics --GE; Phosphoproteins--metabolism--ME; Phosphotyrosine--metabolism--ME; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Stem Cell Factor--pharmacology--PD

CAS Registry No.: 0 (Fusion Proteins, bcr-abl); 0 (Phosphoproteins); 0 (Stem Cell Factor); 21820-51-9 (Phosphotyrosine)

Record Date Created: 19971016

Record Date Completed: 19971016

12/9/6 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0013117280 BIOSIS NO.: 200100289119

Cloning and characterization of a novel cytokine-inducible protein(P29)

AUTHOR: Fukuda Seiji (Reprint); Wu Ding W; Pelus Louis M (Reprint)

AUTHOR ADDRESS: Microbiology/Immunology, Indiana University School of Medicine, Indianapolis, IN, USA**USA
JOURNAL: Blood 96 (11 Part 2): p138b November 16, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Hematopoietic cytokines provide essential stimuli for cell proliferation, differentiation and survival or death. We identified a novel cytokine inducible protein in cell lysates from the Epo-dependent human leukemia cell line, UT7/Epo, using 2-D gel analysis. Compared to Epo-deprived cells, a unique 29kDa spot was consistently observed in lysates from Epo-stimulated cells. After proteolysis and HPLC separation, two peptide sequences were obtained by MALDI-MS that matched a single unknown cDNA in dbEST. The entire ORF was constructed from dbEST consisting of 210 amino acids with a predicted MW of 24kDa. Although P29 lacks known motifs, the N-terminal 45 amino acids show 50% homology with human heterogenous nuclear ribonucleoprotein U (hnRNP) which is associated with messenger RNA processing. P29 is a hydrophilic protein, which is localized in the nucleus as revealed by P29-GFP fusion protein expression in HEK293 cells. P29 has nine potential serine threonine phosphorylation sites and three potential N-glycosylation sites. The gene has at least 9 exons, locates to the long arm of human chromosome 12 and is highly evolutionary conserved from zebrafish to human. It is expressed in most human tissues, indicating that its expression is not unique to Epo. P29 mRNA is high in fetal liver, adult marrow and cardiac muscle, but barely detectable in peripheral blood. Fetal tissues express significantly higher P29 mRNA than adult tissues, and P29 mRNA is several fold higher in cancer cells, particularly leukemia and lymphoma. We have confirmed the expression of P29 mRNA in UT7/Epo cells upon Epo addition and in Mo7e cells upon addition of GM-CSF. Furthermore, removal of Epo from UT7/Epo cells results in reduction of P29 mRNA, cell cycle arrest at G0/G1 and induction of apoptosis. Re-addition of Epo stimulates re-expression of P29 mRNA concomitant with cell cycle progression, suggesting that P29 expression is cell cycle related. P29 overexpression and antisense constructs in HEK293 cells confirm a role for P29 in cell cycle. Synchronization studies in mouse 3T3 cells demonstrated that P29 mRNA remains low in G0/G1, but is dramatically up regulated upon entry into S-Phase. In HL-60 cells FACS sorted with respect to cell cycle, high P29 mRNA expression in S and G2/M phase cells was observed. We also observed up regulation of P29 mRNA in cord blood CD34+ cells following stimulation by the cytokines SCF, Tpo and Flt3 ligand. These results identify P29 as a new protein that plays a role in proliferation and/or survival of normal hematopoietic and cancer cells.

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology; Blood and Lymphatics--Transport and Circulation
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: HEK293 cell line (Hominidae); UT7/Epo cell line (Hominidae)--human leukemia cells
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: Epo {erythropoietin}; p29--characterization,

cloning, cytokine-inducible protein; p29 messenger RNA
MISCELLANEOUS TERMS: cell cycle; cell death; cell differentiation; cell proliferation; cell survival; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
10060 Biochemistry studies - General
00520 General biology - Symposia, transactions and proceedings
02502 Cytology - General
02508 Cytology - Human
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
BIOSYSTEMATIC CODES:
86215 Hominidae

12/9/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13638328 EMBASE No: 2006116377
Targeting leukemic fusion proteins with small interfering RNAs: Recent advances and therapeutic potentials
Thomas M.; Greil J.; Heidenreich O.
O. Heidenreich, Department of Molecular Biology, Interfaculty Institute for Cell Biology, Eberhard Karls University Tuebingen, Aufder Morgenstelle 15, 72076 Tuebingen Germany
AUTHOR EMAIL: olaf.heidenreich@uni-tuebingen.de
Acta Pharmacologica Sinica (ACTA PHARMACOL. SIN.) (United Kingdom)
2006, 27/3 (273-281)
CODEN: CYLPD ISSN: 1671-4083 eISSN: 1745-7254
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 73

RNA interference has become an indispensable research tool to study gene functions in a wide variety of organisms. Because of their high efficacy and specificity, RNA interference-based approaches may also translate into new therapeutic strategies to treat human diseases. In particular, oncogenes such as leukemic fusion proteins, which arise from chromosomal translocations, are promising targets for such gene silencing approaches, because they are exclusively expressed in pre-cancerous and cancerous tissues, and because they are frequently indispensable for maintaining the malignant phenotype. This review summarizes recent developments in targeting leukemia-specific genes and discusses problems and approaches for possible clinical applications. (c)2006 CPS and SIMM.

BRAND NAME/MANUFACTURER NAME: gleevec; sti 571
DRUG DESCRIPTORS:
*small interfering RNA--drug combination--cb; *small interfering RNA--drug therapy--dt; *small interfering RNA--pharmacology--pd; *hybrid protein --endogenous compound--ec
RNA induced silencing complex; BCR ABL protein--endogenous compound--ec; imatinib--drug combination--cb; imatinib--drug therapy--dt; imatinib --pharmacology--pd; rapamycin--drug therapy--dt; Flt3 ligand--endogenous compound--ec; mixed lineage leukemia protein--endogenous compound--ec; steroid receptor coactivator 1--endogenous compound--ec; protein kinase Lyn --endogenous compound--ec; transcription factor RUNX1--endogenous compound --ec; nucleoplasmin--endogenous compound--ec; anaplastic lymphoma kinase --endogenous compound--ec; protein tyrosine kinase--endogenous compound--ec ; unclassified drug
MEDICAL DESCRIPTORS:

*leukemia--drug resistance--dr; *leukemia--drug therapy--dt; *RNA interference
gene targeting; genetic transfection; gene silencing; chronic myeloid leukemia--drug therapy--dt; chronic myeloid leukemia--etiology--et; chromosome translocation; lentivirus vector; myelomonocytic leukemia--drug therapy--dt; large cell lymphoma--drug therapy--dt; drug efficacy; drug specificity; lymphatic leukemia--drug therapy--dt; myeloid leukemia--drug therapy--dt; drug effect; treatment outcome; RNA degradation; translation regulation; gene mutation; gene delivery system; chromosome translocation 5 ; chromosome translocation 12; cell transformation; apoptosis; antineoplastic activity; chromosome translocation 8; chromosome translocation 21; chromosome translocation 4; chromosome translocation 11; human; review
DRUG TERMS (UNCONTROLLED): aml1 mtg8 fusion protein--endogenous compound --ec; mll af4 fusion protein--endogenous compound--ec
CAS REGISTRY NO.: 152459-95-5, 220127-57-1 (imatinib); 53123-88-9 (rapamycin); 171404-15-2 (Flt3 ligand); 140208-17-9 (protein kinase Lyn) ; 166433-56-3 (anaplastic lymphoma kinase); 80449-02-1 (protein tyrosine kinase)
SECTION HEADINGS:
016 Cancer
022 Human Genetics
025 Hematology
037 Drug Literature Index

12/9/8 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

12390690 EMBASE No: 2003501134
Apoptosis induced by molecular targeting therapy in hematological malignancies
Adachi S.; Leoni L.M.; Carson D.A.; Nakahata T.
Dr. S. Adachi, Department of Pediatrics, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin Sakyo-ku, Kyoto 606-8507 Japan
AUTHOR EMAIL: sadachi@kuhp.kyoto-u.ac.jp
Acta Haematologica (ACTA HAEMATOL.) (Switzerland) 2004, 111/1-2 (107-123)
CODEN: ACHAA ISSN: 0001-5792
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 141

Molecular targeting therapies for hematological malignant diseases such as monoclonal antibodies and small molecules have been reviewed. Imatinib mesylate (STI571) targets the tyrosine kinase activity of the bcr-abl fusion protein in CML, and was superior to IFN-alpha plus low-dose cytarabine in newly diagnosed chronic-phase CML in a phase III randomized study. Imatinib induced apoptosis in bcr-abl-positive cells in vitro, and activates several signaling pathways such as PI3K/Akt, STAT5 and Ras/MAPK. Combination therapies with imatinib and new strategies for downregulation of intracellular Bcr-Abl protein levels have also been investigated from the phenomenon of resistance to imatinib. Anti-CD20 (rituximab) became the first monoclonal antibody approved for the treatment of a relapsed/refractory follicular/low-grade NHL and promising results were obtained from a phase III randomized study. Although antibody-dependent cell-mediated cytotoxicity and complement-mediated cytotoxicity are likely to be the major effectors of B-cell depletion in vivo, direct cytotoxicity

by CD20 monoclonal antibody on B-cell lines in vitro has been reported. Anti-CD33 (Mylotarg) and FLT3 inhibitors for AML have also been used in clinical trials and signaling pathways induced by these agents are under intensive investigation. Arsenic trioxide, like all-trans-retinoic acid (ATRA), downregulates promyelocytic leukemia protein/retinoic acid receptor-alpha (PML/RARalpha) fusion protein and induced apoptosis in APL cells, and promising results were obtained from ATRA-resistant APL patients. Finally we show our promising in vitro and in vivo data of Retodolac (a non-steroidal anti-inflammatory drug lacking cyclooxygenase inhibitor activity) against chronic lymphocytic leukemia (CLL) cells.

BRAND NAME/MANUFACTURER NAME: cep 701; sti 571; pkc 412; su 11248; ct 53518 ; su 5416; aspirin; sdx 101
DRUG DESCRIPTORS:
*imatinib--adverse drug reaction--ae; *imatinib--clinical trial--ct; * imatinib--drug combination--cb; *imatinib--drug comparison--cm; *imatinib --drug therapy--dt; *imatinib--pharmacology--pd; *alpha interferon--adverse drug reaction--ae; *alpha interferon--clinical trial--ct; *alpha interferon --drug combination--cb; *alpha interferon--drug comparison--cm; *alpha interferon--drug therapy--dt; *alpha interferon--pharmacology--pd; * cytarabine--adverse drug reaction--ae; *cytarabine--clinical trial--ct; * cytarabine--drug combination--cb; *cytarabine--drug comparison--cm; * cytarabine--drug dose--do; *cytarabine--drug therapy--dt; *cytarabine --pharmacology--pd; *rituximab--clinical trial--ct; *rituximab--drug combination--cb; *rituximab--drug therapy--dt; *rituximab--pharmacology--pd ; *gemtuzumab ozogamicin--adverse drug reaction--ae; *gemtuzumab ozogamicin --clinical trial--ct; *gemtuzumab ozogamicin--drug therapy--dt; *gemtuzumab ozogamicin--pharmacology--pd
protein kinase B--endogenous compound--ec; STAT5 protein--endogenous compound--ec; mitogen activated protein kinase--endogenous compound--ec; Ras protein--endogenous compound--ec; monoclonal antibody--adverse drug reaction--ae; monoclonal antibody--clinical trial--ct; monoclonal antibody --drug combination--cb; monoclonal antibody--drug comparison--cm; monoclonal antibody--drug therapy--dt; monoclonal antibody--pharmacology --pd; antineoplastic agent--clinical trial--ct; antineoplastic agent--drug therapy--dt; antineoplastic agent--pharmacology--pd; arsenic trioxide --adverse drug reaction--ae; arsenic trioxide--clinical trial--ct; arsenic trioxide--drug therapy--dt; arsenic trioxide--pharmacology--pd; retinoic acid receptor alpha--endogenous compound--ec; retinoic acid--drug therapy --dt; fludarabine--drug combination--cb; fludarabine--drug therapy--dt; bendamustine--drug combination--cb; bendamustine--drug therapy--dt; mitoxantrone--drug combination--cb; mitoxantrone--drug therapy--dt; CD20 antigen--endogenous compound--ec; carbazole derivative--clinical trial--ct; carbazole derivative--drug therapy--dt; carbazole derivative--pharmacology --pd; cep 701--clinical trial--ct; cep 701--drug therapy--dt; cep 701 --pharmacology--pd; staurosporine derivative--clinical trial--ct; staurosporine derivative--drug therapy--dt; staurosporine derivative --pharmacology--pd; etodolac--clinical trial--ct; etodolac--drug comparison --cm; etodolac--drug concentration--cr; etodolac--drug dose--do; etodolac --drug therapy--dt; etodolac--pharmacology--pd; etodolac--oral drug administration--po; nonsteroid antiinflammatory agent--clinical trial--ct; nonsteroid antiinflammatory agent--drug comparison--cm; nonsteroid antiinflammatory agent--drug concentration--cr; nonsteroid antiinflammatory agent--drug dose--do; nonsteroid antiinflammatory agent--drug therapy--dt; nonsteroid antiinflammatory agent--pharmacology--pd; nonsteroid antiinflammatory agent--oral drug administration--po; quinazoline derivative--pharmacology--pd; 3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one--pharmacology--pd; unindexed drug; unclassified drug; acetylsalicylic acid

MEDICAL DESCRIPTORS:
*apoptosis; *hematologic malignancy--drug resistance--dr; *hematologic malignancy--drug therapy--dt; *drug targeting
drug mechanism; enzyme activity; randomized controlled trial; low drug dose ; chronic myeloid leukemia--drug therapy--dt; cell level; nonhodgkin lymphoma--drug therapy--dt; antibody dependent lymphocytotoxicity; lymphocyte depletion; B lymphocyte; receptor down regulation; promyelocytic leukemia--drug resistance--dr; promyelocytic leukemia--drug therapy--dt; acute granulocytic leukemia--drug therapy--dt; skin manifestation--side effect--si; gastrointestinal symptom--side effect--si; musculoskeletal disease--side effect--si; cardiotoxicity--side effect--si; neurotoxicity --side effect--si; drug blood level; human; nonhuman; clinical trial; review; priority journal
DRUG TERMS (UNCONTROLLED): Flt3 ligand inhibitor--clinical trial--ct; Flt3 ligand inhibitor--drug therapy--dt; Flt3 ligand inhibitor--pharmacology--pd ; pkc 412--clinical trial--ct; pkc 412--drug therapy--dt; pkc 412 --pharmacology--pd; su 11248--pharmacology--pd; ct 53518--pharmacology--pd; sdx 101
CAS REGISTRY NO.: 152459-95-5, 220127-57-1 (imatinib); 147-94-4, 69-74-9 (cytarabine); 174722-31-7 (rituximab); 148640-14-6 (protein kinase B); 142243-02-5 (mitogen activated protein kinase); 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6 (arsenic trioxide); 302-79-4 (retinoic acid); 21679-14-1 (fludarabine); 16506-27-7, 3543-75-7 (bendamustine); 65271-80-9, 70476-82-3 (mitoxantrone); 111358-88-4, 156256-78-9 (cep 701); 41340-25-4 (etodolac); 186610-95-7 (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one); 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1 (acetylsalicylic acid)
SECTION HEADINGS:
016 Cancer
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reaction Titles

12/9/9 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

12305505 EMBASE No: 2003411278
FLT3 expressing leukemias are selectively sensitive to inhibitors of the molecular chaperone heat shock protein 90 through destabilization of signal transduction-associated kinases
Yao Q.; Nishiuchi R.; Li Q.; Kumar A.R.; Hudson W.A.; Kersey J.H.
J.H. Kersey, Cancer Center, University of Minnesota, MMC 86, 420 Delaware Street, Minneapolis, MN 55455 United States
AUTHOR EMAIL: kerse001@umn.edu
Clinical Cancer Research (CLIN. CANCER RES.) (United States) 01 OCT 2003, 9/12 (4483-4493)
CODEN: CCREF ISSN: 1078-0432
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

Purpose: We conducted studies to evaluate the hypothesis that FLT3 is a client of heat shock protein (Hsp) 90 and inhibitors of Hsp90 may be useful for therapy of leukemia. Experimental Design: The effects of the Hsp90-inhibitor 17-allylamino-17-demethoxygeldanamycin (17-AAG) on cell growth, expression of signal transduction kinases, apoptosis, FLT3 phosphorylation and interaction with Hsp90 was determined in FLT3SUP+ human

leukemias. Results: We found that FLT3 is included in a multi-protein complex that includes Hsp90 and p23. 17-AAG inhibited FLT3 phosphorylation and interaction with Hsp90. FLT3 SUP+ leukemias were significantly more sensitive to the Hsp90 inhibitors 17-AAG and Herbimycin A in cell growth assays than FLT3-negative leukemias. Cells transfected with FLT3 became sensitive to 17-AAG. Cell cycle inhibition and apoptosis were induced by 17-AAG. Cells with constitutive expression of FLT3, as a result of internal tandem duplication, were the most sensitive; cells with wild-type FLT3 were intermediate in sensitivity, and FLT3-negative cells were the least sensitive. 17-AAG resulted in reduced cellular mass of FLT3, RAF, and AKT. The mass of another Hsp, Hsp70, was increased. The expression level of MLL-AF4 fusion protein was not reduced by 17-AAG in human leukemia cells. Conclusions: FLT3SUP+ leukemias are sensitive to 17-AAG and Herbimycin A. 17-AAG inhibits leukemia cells with either FLT3-internal tandem duplication or wild-type FLT3, in part through destabilization of client kinases including FLT3, RAF, and AKT. 17-AAG is potentially useful for therapy of FLT3-expressing leukemias, including the mixed lineage leukemia fusion gene leukemias.

MANUFACTURER NAMES: National Institute of Health/United States
DRUG DESCRIPTORS:
*Flt3 ligand--endogenous compound--ec; *heat shock protein 90--endogenous compound--ec; *phosphotransferase--endogenous compound--ec chaperone--endogenous compound--ec; protein p23--endogenous compound--ec; geldanamycin--drug development--dv; geldanamycin--pharmacology--pd; herbimycin A--drug development--dv; herbimycin A--pharmacology--pd; Raf protein--endogenous compound--ec; protein kinase B--endogenous compound--ec ; heat shock protein 70--endogenous compound--ec; hybrid protein; mixed lineage leukemia protein--endogenous compound--ec; unclassified drug
MEDICAL DESCRIPTORS:
*leukemia--diagnosis--di; *protein expression; *enzyme stability evaluation; inhibition kinetics; cancer inhibition; cell growth; signal transduction; apoptosis; protein phosphorylation; protein interaction; complex formation; genetic transfection; drug sensitivity; gene expression; tandem repeat; wild type; cell specificity; human; controlled study; human cell; article; priority journal
DRUG TERMS (UNCONTROLLED): heat shock protein 90 inhibitor--drug development--dv; heat shock protein 90 inhibitor--pharmacology--pd; signal transduction associated kinase--endogenous compound--ec; 17 allylamino 17 demethoxygeldanamycin--drug development--dv; 17 allylamino 17 demethoxygeldanamycin--pharmacology--pd; mll af4 fusion protein
CAS REGISTRY NO.: 171404-15-2 (Flt3 ligand); 9031-09-8, 9031-44-1 (phosphotransferase); 30562-34-6 (geldanamycin); 70563-58-5 (herbimycin A); 148640-14-6 (protein kinase B)
SECTION HEADINGS:
016 Cancer
025 Hematology
037 Drug Literature Index

12/9/10 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

11122788 EMBASE No: 2001139362
ARG tyrosine kinase activity is inhibited by STI571
Okuda K.; Weisberg E.; Gilliland D.G.; Griffin J.D.
J.D. Griffin, Department of Adult Oncology, Dana Farber Cancer Institute, 44 Binney Street, Boston, MA 02115 United States
AUTHOR EMAIL: james griffin@dfci.harvard.edu

Blood (BLOOD) (United States) 15 APR 2001, 97/8 (2440-2448)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 40

The tyrosine kinase inhibitor STI571 inhibits BCR/ABL and induces hematologic remission in most patients with chronic myeloid leukemia. In addition to BCR/ABL, STI571 also inhibits v-Abl, TEL/ABL, the native platelet-derived growth factor (PDGF)beta receptor, and c-KIT, but it does not inhibit SRC family kinases, c-FMS, FLT3, the epidermal growth factor receptor, or multiple other tyrosine kinases. ARG is a widely expressed tyrosine kinase that shares substantial sequence identity with c-ABL in the kinase domain and cooperates with ABL to regulate neurulation in the developing mouse embryo. As described here, ARG has recently been implicated in the pathogenesis of leukemia as a fusion partner of TEL. A TEL/ARG fusion was constructed to determine whether ARG can be inhibited by STI571. When expressed in the factor-dependent murine hematopoietic cell line Ba/F3, the TEL/ARG protein was heavily phosphorylated on tyrosine, increased tyrosine phosphorylation of multiple cellular proteins, and induced factor-independent proliferation. The effects of STI571 on Ba/F3 cells transformed with BCR/ABL, TEL/ABL, TEL/PDGFbetaR, or TEL/ARG were then compared. STI571 inhibited tyrosine phosphorylation and cell growth of Ba/F3 cells expressing BCR/ABL, TEL/ABL, TEL/PDGFbetaR, and TEL/ARG with an ICSUB50 of approximately 0.5 muM in each case, but it had no effect on untransformed Ba/F3 cells growing in IL-3 or on Ba/F3 cells transformed by TEL/JAK2. Culture of TEL/ARG-transfected Ba/F3 cells with IL-3 completely prevented STI571-induced apoptosis in these cells, similar to what has been observed with BCR/ABL- or TEL/ABL-transformed cells. These results indicate that ARG is a target of the small molecule, tyrosine kinase inhibitor STI571. (c) 2001 by The American Society of Hematology.

BRAND NAME/MANUFACTURER NAME: sti 571
DRUG DESCRIPTORS:
*protein tyrosine kinase inhibitor--drug analysis--an; *protein tyrosine kinase inhibitor--drug development--dv; *protein tyrosine kinase inhibitor --drug dose--do; *protein tyrosine kinase inhibitor--pharmacology--pd; *2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine--drug analysis--an; *2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine--drug development--dv; *2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine--pharmacology --pd; *platelet derived growth factor beta receptor
platelet derived growth factor; stem cell factor; Flt3 ligand; epidermal growth factor receptor; annexin
MEDICAL DESCRIPTORS:
*enzyme activity
remission; myeloid leukemia; enzyme inhibition; leukemia remission; neurulation; pathogenesis; gene fusion; protein phosphorylation; cell growth; cell transformation; nonhuman; mouse; animal cell; article; priority journal
CAS REGISTRY NO.: 152459-95-5 (2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine); 171404-15-2 (Flt3 ligand)
SECTION HEADINGS:
025 Hematology
037 Drug Literature Index

12/9/11 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

12746147 Genuine Article#: 817AN Number of References: 34
Title: Inducible release of TRAIL fusion proteins from a proapoptotic form for tumor therapy
Author(s): Shah K (REPRINT) ; Tung CH; Yang K; Weissleder R; Breakefield XO
Corporate Source: Massachusetts Gen Hosp,Dept Neurol, Mol Neurogenet Unit,13th St,Bldg 149/Charlestown//MA/02129 (REPRINT); Harvard Univ,Sch Med, Mol Neurogenet Unit, Dept Neurol,Boston//MA/; Harvard Univ,Sch Med , Ctr Mol Imaging Res, Massachusetts Gen Hosp,Boston//MA/
Journal: CANCER RESEARCH, 2004, V64, N9 (MAY 1), P3236-3242
ISSN: 0008-5472 Publication date: 20040501
Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA
Language: English Document Type: ARTICLE
Geographic Location: USA
Journal Subject Category: ONCOLOGY
Abstract: Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) can selectively kill neoplastic cells and control of its activity could enhance tumor therapy. We have developed means to control the secretion of a novel recombinant (r) TRAIL fusion protein using a viral protease. This system uses the endoplasmic reticulum (ER) as a storage depot for rTRAIL, because TRAIL acts by binding to its cognate receptors on the cell surface. We have engineered two TRAIL variants: (a) a secretable form that enhances apoptosis via a bystander effect; and (b) an ER-targeted TRAIL that is retained in the ER until selectively released by the viral protease. Gene delivery can be monitored in vivo by systemic administration of a near infrared fluorescent (NIRF) probe activated by the protease. This study serves as a template for design of recombinant proteins to enhance and control apoptosis of tumor cells via specific viral proteases and for use of viral proteases as in vivo reporters for cancer therapy.
Identifiers--KeyWord Plus(R): IN-VIVO; ENDOPLASMIC-RETICULUM; ANTITUMOR-ACTIVITY; MOLECULAR-CLONING; DECOY RECEPTORS; DEATH DOMAIN; LIGAND TRAIL; FLT3 LIGAND; APOPTOSIS; CELLS
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    WU XF, 2001, V3, P368, MOL THER
?


Set     Items   Description
S1       5254   (FLT3 (W) LIGAND)
S2       1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3          8   S1 AND S2
S4          4   RD S3  (unique items)
S5         80   (S1 AND CHIMERA)
S6         52   RD S5  (unique items)
S7      39485   (APOPTOSIS AND ANTIBODY)
S8          1   S7 AND S6
S9        121   (S1 AND (FUSION (W) PROTEIN))
S10        60   RD S9  (unique items)
S11        11   (S10 AND APOPTOSIS)
S12        11   RD S11  (unique items)
?

S (P230 (W) ANTIBODY)
             425  P230
         1758699  ANTIBODY
     S13       0  (P230 (W) ANTIBODY)
?

S SM5 (W) ANTIBODY
             230  SM5
         1758699  ANTIBODY
     S14       0  SM5 (W) ANTIBODY
?


Set     Items   Description
S1       5254   (FLT3 (W) LIGAND)
S2       1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3          8   S1 AND S2
S4          4   RD S3  (unique items)
S5         80   (S1 AND CHIMERA)
S6         52   RD S5  (unique items)
S7      39485   (APOPTOSIS AND ANTIBODY)
S8          1   S7 AND S6
S9        121   (S1 AND (FUSION (W) PROTEIN))
S10        60   RD S9  (unique items)
S11        11   (S10 AND APOPTOSIS)
S12        11   RD S11  (unique items)
S13         0   (P230 (W) ANTIBODY)
S14         0   SM5 (W) ANTIBODY
?

S (P (W) 230)
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         7231836  P
           62459  230
     S15     396  (P (W) 230)
?

S S15 AND ANTIBODY
            396  S15
         1758699  ANTIBODY
     S16       2  S15 AND ANTIBODY
?

RD S16
     S17       2  RD S16  (unique items)
?

TYPE S17/FULL/1-2

  17/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

06451491   PMID: 6205675
 Distribution of p230, an alpha-spectrin-related polypeptide in normal and
 psoriatic epidermis and in cultured human keratinocytes.
  Kariniemi A L; Lehto V P; Virtanen I
  British journal of dermatology (ENGLAND)   Aug 1984,  111  (2)  p139-45,
ISSN 0007-0963--Print   Journal Code: 0004041
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Subfile:   INDEX MEDICUS
  We studied the localization of p230, an immunoanalogue of erythroid
alpha-spectrin, in normal and psoriatic human epidermis and in cultured
human keratinocytes. In immunofluorescence microscopy of frozen sections of
normal skin a bright cytoplasmic staining was seen in the cortical area of
the keratinocytes. Similar staining was also seen in lesional and
uninvolved areas of psoriatic epidermis. The pericytoplasmic localization
of p230 could also be seen in cultured human keratinocytes: a lamina-like
reticular staining was seen mostly confined to the ventral cytoplasmic
aspect and to junctional areas of the cells. Immunoblotting of
electrophoretically separated polypeptides of epidermal cells revealed a
distinct polypeptide of Mr 230 kD. The results indicate that
alpha-spectrin-like polypeptides form a major cytoskeletal framework in
human epidermal cells in both normal and psoriatic skin.
  Descriptors: *Epidermis--analysis--AN; *Peptides--analysis--AN; *Psoriasi
s--metabolism--ME; Cells, Cultured; Epidermis--cytology--CY; Fluorescent
Antibody Technique; Humans; Keratin--biosynthesis--BI; Research Support,
Non-U.S. Gov't
  CAS Registry No.: 0   (Peptides); 0   (p 230); 68238-35-7   (Keratin)
  Record Date Created: 19840928
  Record Date Completed: 19840928


  17/9/2     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0007707194   BIOSIS NO.: 199191090085
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CORRECTION OF BA 90092518. CURRENT DATA ON PREVALENCE AND EPIDEMIOLOGY OF HIV FROM THE HIV-STUDY OF THE RED CROSS BLOOD BANKS IN WEST GERMANY. ADDITION OF AUTHOR NAMES. ERRATUM PUBLISHED IN INFUSIONSTHERAPIE VOL. 17. ISS. 4. 1990. P.230

AUTHOR: GLUECK D (Reprint); KUBANEK B; GAUS W; ELBERT G; GRAESSMANN W; HESSE R; HOLZBERGER G; KOERNER K; PEICHL-HOFFMANN G; ET AL
AUTHOR ADDRESS: ABT TRANSFUSIONSMEDIZIN, UNIV ULM, DRK-BLUTSPENDEZENTRALE, HELMHOLTZSTR 10, D-7900 ULM, BRD**GERMANY
JOURNAL: Infusionstherapie 17 (3): p160-162 1990
ISSN: 1011-6966
DOCUMENT TYPE: Article; Errata
RECORD TYPE: Abstract
LANGUAGE: GERMAN

ABSTRACT: From the multicenter study of the Red Cross Blood Banks in the FRG HIV-antibody prevalences and incidences are documented since July 1985. Constantly low prevalences and incidences since 1987 of less than 2 Western blot (Wb)-positive donors and less than 1 Wb-positive donor per 100,000 donors respectively confirm our estimate of the rest risk of an HIV-infection by blood products of 1:500,000 to 1:3 million donations. In the epidemiologic details there seems to be a trend to an increase of the incidence in male repeat blood donors. The modes of HIV-infection in blood donors have changed to an increasing number of infections acquired in heterosexual contacts to persons at risk.

DESCRIPTORS: CORRECTED ARTICLE HUMAN IMMUNODEFICIENCY VIRUS HUMAN
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Clinical Endocrinology--Human Medicine, Medical Sciences; Epidemiology--Population Studies; Infection; Public Health--Allied Medical Sciences
BIOSYSTEMATIC NAMES: Retroviridae--DNA and RNA Reverse Transcribing Viruses, Viruses, Microorganisms; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
COMMON TAXONOMIC TERMS: DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses; Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CONCEPT CODES:
15001 Blood - General and methods
33506 Virology - Animal host viruses
34508 Immunology - Immunopathology, tissue immunology
36006 Medical and clinical microbiology - Virology
37010 Public health - Public health administration and statistics
37052 Public health: epidemiology - Communicable diseases
37400 Public health: microbiology - Public health microbiology
BIOSYSTEMATIC CODES:
03305 Retroviridae
86215 Hominidae
?

Set	Items	Description
S1	5254	(FLT3 (W) LIGAND)
S2	1166	(CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3	8	S1 AND S2
S4	4	RD S3 (unique items)
S5	80	(S1 AND CHIMERA)
S6	52	RD S5 (unique items)
S7	39485	(APOPTOSIS AND ANTIBODY)
S8	1	S7 AND S6
S9	121	(S1 AND (FUSION (W) PROTEIN))

```
S10         60   RD S9  (unique items)
S11         11   (S10 AND APOPTOSIS)
S12         11   RD S11  (unique items)
S13          0   (P230 (W) ANTIBODY)
S14          0   SM5 (W) ANTIBODY
S15        396   (P (W) 230)
S16          2   S15 AND ANTIBODY
S17          2   RD S16  (unique items)
?

S (SM5 (W) 1)
              230  SM5
         15677846  1
     S18       30  (SM5 (W) 1)
?

RD S18
     S19       11  RD S18  (unique items)
?
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?

TYPE S19/FULL/1-11

  19/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

20762038   PMID: 16567969
 Concordant loss of melanoma differentiation antigens in synchronous and
 asynchronous melanoma metastases: implications for immunotherapy.
  Trefzer Uwe; Hofmann Maja; Reinke Susanne; Guo Ya-Jun; Audring Heike;
Spagnoli Giulio; Sterry Wolfram
  Department of Dermatology and Allergy, Skin Cancer Centre,
Charite-Universitatsmedizin Berlin, Berlin, Germany. uwe.trefzer@charite.de
  Melanoma research (England) Apr 2006, 16 (2) p137-45, ISSN
0960-8931--Print  Journal Code: 9109623
  Publishing Model Print
  Document type: Journal Article
```

Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS

Because of its known heterogeneity, the analysis of antigen expression is crucial prior to the initiation of antigen-specific immunotherapy for melanoma. The melanoma differentiation antigens gp100, MART-1 and tyrosinase are involved in a common pathway of melanin synthesis. Peptides derived from these melanoma differentiation antigens are used in the immunotherapy of melanoma and antibodies recognizing these antigens are commonly applied to detect melanocytic lesions. One hundred and ninety-one paraffin-embedded melanoma metastases from 28 patients with 2-19 lesions (mean, 6.8) developing synchronously (n = 67) or asynchronously (n = 124) were analysed by immunohistochemistry for the expression of the melanoma differentiation antigens, as well as cancer/testis antigens of the melanoma antigen-A (MAGE-A) family (monoclonal antibodies 77B and 57B), anti-S100 and SM5-1. The overall reactivities were 81.6% (gp100), 79.5% (MART-1), 59.6% (tyrosinase), 59.1% (77B), 60.7% (57B), 93.2% (S100) and 91.6% (SM5-1). Twenty-seven lesions (14.1%) were positive for all tumour-associated antigens, 75 lesions (39.2%) were negative for one antigen and 87 lesions (45.5%) were negative for several tumour-associated antigens. Co-ordinated loss was found for lesions negative for gp100 and MART-1 (9.4%, P < 0.0005), gp100 and tyrosinase (11.0%, P = 0.009), MART-1 and tyrosinase (15.2%, P < 0.0005) and gp100, MART-1 and tyrosinase (8.9%, P < 0.0005), which is up to six times higher than the expected calculated loss. This co-ordinated loss of melanoma differentiation antigens in melanoma did not include cancer testis antigens and S100 or SM5-1. On average, the melanoma differentiation antigens stained 50-65% of cells within a lesion, and 10-39% of synchronous clusters were heterogeneous for melanoma differentiation antigen expression. In conclusion, broader polypeptide vaccines should be used for melanoma immunotherapy.

Record Date Created: 20060328

19/9/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

19941287 PMID: 16405722

The monoclonal antibody SM5-1 recognizes a fibronectin variant which is widely expressed in melanoma.

Trefzer Uwe; Chen Yingwen; Herberth Gunda; Hofmann Maja Ann; Kiecker Felix; Guo Yajun; Sterry Wolfram

Department of Dermatology and Allergy, Skin Cancer Center, Charite - Universitatsmedizin Berlin, Schumannstrasse 20/21, 10117 Berlin, Germany. uwe.trefzer@charite.de

BMC cancer electronic resource (England) 2006, 6 p8, ISSN 1471-2407 --Electronic Journal Code: 100967800

Publishing Model Electronic
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

BACKGROUND: Previously we have generated the monoclonal antibody SM5-1 by using a subtractive immunization protocol of human melanoma. This antibody exhibits a high sensitivity for primary melanomas of 99% (248/250 tested) and for metastatic melanoma of 96% (146/151 tested) in paraffin embedded sections. This reactivity is superior to the one obtained by HMB-45, anti-MelanA or anti-Tyrosinase and is comparable to anti-S100. However, as

compared to anti-S100, the antibody SM5-1 is highly specific for melanocytic lesions since 40 different neoplasms were found to be negative for SM5-1 by immunohistochemistry. The antigen recognized by SM5-1 is unknown. METHODS: In order to characterize the antigen recognized by mAb SM5-1, a cDNA library was constructed from the metastatic human melanoma cell line SMMUpos in the Uni-ZAP lambda phage and screened by mAb SM5-1. The cDNA clones identified by this approach were then sequenced and subsequently analyzed. RESULTS: Sequence analysis of nine independent overlapping clones (length 3100-5600 bp) represent fibronectin cDNA including the ED-A, but not the ED-B region which are produced by alternative splicing. The 89aa splicing variant of the IIICS region was found in 8/9 clones and the 120aa splicing variant in 1/9 clones, both of which are included in the CS1 region of fibronectin being involved in melanoma cell adhesion and spreading. CONCLUSION: The molecule recognized by SM5-1 is a melanoma associated FN variant expressed by virtually all primary and metastatic melanomas and may play an important role in melanoma formation and progression. This antibody is therefore not only of value in immunohistochemistry, but potentially also for diagnostic imaging and immunotherapy.

Descriptors: *Antibodies, Monoclonal--immunology--IM; *Antigens, Neoplasm --immunology--IM; *Fibronectins--immunology--IM; *Melanoma--immunology--IM; *Skin Neoplasms--immunology--IM; Alternative Splicing; Cell Adhesion; Flow Cytometry; Gene Library; Humans; Immunohistochemistry; Melanoma --physiopathology--PP; Research Support, Non-U.S. Gov't; Skin Neoplasms --physiopathology--PP

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antigens, Neoplasm); 0 (Fibronectins)

Record Date Created: 20060126

Record Date Completed: 20060221

Date of Electronic Publication: 20060111

19/9/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

19598518 PMID: 16148409

Differential expression of MART-1, tyrosinase, and SM5-1 in primary and metastatic melanoma.

Reinke Susanne; Koniger Peter; Herberth Gunda; Audring Heike; Wang Hao; Ma Jing; Guo Yajun; Sterry Wolfram; Trefzer Uwe

Department of Dermatology and Allergy, Skin Cancer Centre, Charite-Universitaetsmedizin Berlin, Germany.

American Journal of dermatopathology (United States) Oct 2005, 27 (5) p401-6, ISSN 0193-1091--Print Journal Code: 7911005

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The new monoclonal antibody SM5-1 has been shown to have significant advantages in immunohistochemistry of melanoma over currently used antibodies such as HMB-45 or anti-S100. In this study we compared the immunohistological staining pattern of SM5-1 with that of the more recently described antibodies A103 (anti-MART-1) and T311 (anti-Tyrosinase) in 344 paraffin-embedded melanoma specimens, consisting of 101 primary melanomas (77 SSM, 16 NM, 6 ALM, 2 LMM) and 243 melanoma metastases. The overall reactivity of SM5-1 for all the specimens was 92% (318/344) compared with 83% (285/344) for MART-1 and 71% (245/344) for Tyrosinase. Staining of

melanoma metastases with SM5-1 was found in 91% (222/243), but only in 77% (187/243) with A103 and 63% (154/243) with T311, respectively. Staining with SM5-1 was more homogenous with 196 of 243 (80%) of metastatic lesions showing 50% or more positively stained cells within the lesions, whereas A103 and T311 did so in 141 of 243 (58%) or 117 of 243 (48%) of the lesions. With regard to staining intensity of SM5-1, 157 of 243 (64%) showed a strong or very strong staining intensity, whereas A103 and T311 did so in 85 of 243 (35%) or 70 of 243 (29%) of the lesions. Staining intensity and percentage positivity correlated well for SM5-1, because from the 58 very strong positive metastases 55 showed staining in more than 75% of the cells within a lesion. Importantly, 52 of 56 MART-1-negative metastases and 81 of 89 Tyrosinase-negative metastases were positive for SM5-1. Thirty-eight metastases (15.6%) were negative for both A103 and T311. Of those, 35 (92.1%) were positive for SM5-1, demonstrating the value of SM5-1 in identifying melanoma-associated antigen-negative lesions. We conclude that SM5-1 could be of value in immunohistochemistry of melanoma.

Descriptors: *Antibodies, Monoclonal--diagnostic use--DU; *Antigens, Neoplasm--biosynthesis--BI; *Melanoma--immunology--IM; *Monophenol Monooxygenase--biosynthesis--BI; *Neoplasm Proteins--biosynthesis--BI; *Skin Neoplasms--immunology--IM; Comparative Study; Humans; Immunohistochemistry; Melanoma--pathology--PA; Neoplasm Metastasis --immunology--IM; Research Support, Non-U.S. Gov't; Skin Neoplasms --pathology--PA; Tumor Markers, Biological--analysis--AN

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antigens, Neoplasm); 0 (Melan-A protein); 0 (Neoplasm Proteins); 0 (Tumor Markers, Biological)

Enzyme No.: EC 1.14.18.1 (Monophenol Monooxygenase)

Record Date Created: 20050908

Record Date Completed: 20051220

19/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13016937 PMID: 11214818

SM5-1: a new monoclonal antibody which is highly sensitive and specific for melanocytic lesions.

Trefzer U; Rietz N; Chen Y; Audring H; Herberth G; Siegel P; Reinke S; Koniger P; Wu S; Ma J; Liu Y; Wang H; Sterry W; Guo Y

Department of Dermatology and Allergy, Charite, Humboldt University Berlin, Germany. uwe.trefzer@charite.de

Archives of dermatological research (Germany) Dec 2000, 292 (12) p583-9, ISSN 0340-3696--Print Journal Code: 8000462

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Antibodies such as HMB-45 and anti-S100 protein have been widely used as markers of malignant melanoma despite evidence that HMB-45 has a sensitivity of only 67-93% and S100 is nonspecific for melanoma. Using a subtractive immunization protocol in a mouse model of human melanoma, we have generated several monoclonal antibodies with putative specificity for melanoma. After initial screenings, the antibody SM5-1 was chosen because of its intriguing reactivity with melanocytic tumors in both frozen and paraffin sections. The immunohistochemical staining of SM5-1 was studied in paraffin-embedded specimens of 401 melanomas (n = 401; 250 primary melanomas, 151 metastases), melanocytic nevi of the skin (n = 16),

nonmelanocytic neoplasms (n = 84). The results were compared with HMB-45 and anti-S100 staining. All antibodies reacted with nevi and 97-99% with primary melanomas. Whereas both SM5-1 and anti-S100 stained 96% (146/151) of melanoma metastases, HMB-45 correctly identified only 83% (126/151). All HMB-45-negative metastases were positive for SM5-1. Whereas neither SM5-1 nor HMB-45 stained any of 84 specimens from 40 different nonmelanocytic neoplasms, anti-S100 was positive in 21/84 (25%). While the staining pattern of SM5-1 was mostly homogeneous, small tumor areas in some metastases remained unstained. Staining with SM5-1 was also observed in perivascular dendritic cells, in plasma cells, some myofibroblasts and the secretion of eccrine sweat glands. Nonactivated epidermal melanocytes, keratinocytes, endothelial cells, smooth muscle cells and peripheral nerves were all negative for SM5-1. These results suggest that SM5-1 is highly specific, as well as sensitive, for melanocytic lesions and is useful in the immunohistochemical evaluation of melanoma.

Descriptors: *Antibodies, Monoclonal--diagnostic use--DU; *Melanoma --diagnosis--DI; Animals; Antibodies, Monoclonal--biosynthesis--BI; Comparative Study; Disease Models, Animal; Humans; Hybridomas; Immunohistochemistry; Lymphatic Metastasis--diagnosis--DI; Lymphatic Metastasis--pathology--PA; Melanoma--immunology--IM; Melanoma--secondary --SC; Mice; Neoplasm Metastasis--diagnosis--DI; Neoplasm Metastasis --immunology--IM; Nevus, Pigmented--chemistry--CH; Nevus, Pigmented --diagnosis--DI; Nevus, Pigmented--pathology--PA; Research Support, Non-U.S. Gov't; Sensitivity and Specificity; Skin Neoplasms--diagnosis--DI; Skin Neoplasms--immunology--IM; Skin Neoplasms--pathology--PA

CAS Registry No.: 0 (Antibodies, Monoclonal)

Record Date Created: 20010214

Record Date Completed: 20010503

19/9/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10420809 PMID: 7706785

Intranasal immunization with recombinant group A streptococcal M protein fragment fused to the B subunit of Escherichia coli labile toxin protects mice against systemic challenge infections.

Dale J B; Chiang E C

Department of Veterans Affairs Medical Center, Memphis, TN 38104.

Journal of infectious diseases (UNITED STATES) Apr 1995, 171 (4) p1038-41, ISSN 0022-1899--Print Journal Code: 0413675

Contract/Grant No.: AI-10085; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: AIM; INDEX MEDICUS

A fusion gene named LT-B-M5 was constructed encoding the entire B subunit of Escherichia coli labile toxin (LT-B), a 7 amino acid proline-rich linker, and 15 amino-terminal amino acids of type 5 streptococcal M protein. The purified LT-B-M5 was immunogenic in rabbits and evoked antibodies against a synthetic peptide copy of the amino-terminus of M5 (SM5[1-15]) and the native M5 protein and opsonic antibodies against type 5 streptococci. The hybrid protein retained the ganglioside-binding activity of LT-B and was tested in mice for its immunogenicity after local administration. Mice that were immunized intranasally with LT-B-M5 developed serum antibodies against SM5(1-15) and were significantly protected from death after intraperitoneal challenge infections with type 5

streptococci. The data show that protective systemic immune responses may be evoked after intranasal immunization with a fragment of M protein fused to LT-B.

Tags: Female

Descriptors: *Antigens, Bacterial--immunology--IM; *Bacterial Outer Membrane Proteins; *Bacterial Proteins--immunology--IM; *Bacterial Toxins --immunology--IM; *Bacterial Vaccines--immunology--IM; *Carrier Proteins; *Enterotoxins--immunology--IM; *Escherichia coli Proteins; *Recombinant Fusion Proteins--immunology--IM; *Streptococcal Infections--prevention and control--PC; *Streptococcus--immunology--IM; Administration, Intranasal; Animals; Antibodies, Bacterial--biosynthesis--BI; Antibodies, Bacterial --blood--BL; Bacterial Proteins--genetics--GE; Bacterial Toxins--genetics --GE; Bacterial Toxins--metabolism--ME; Bacterial Vaccines--administration and dosage--AD; Base Sequence; Enterotoxins--genetics--GE; Enterotoxins --metabolism--ME; Escherichia coli--genetics--GE; Gangliosides--metabolism --ME; Mice; Mice, Inbred BALB C; Molecular Sequence Data; Rabbits; Recombinant Fusion Proteins--administration and dosage--AD; Recombinant Fusion Proteins--isolation and purification--IP; Recombinant Fusion Proteins--metabolism--ME; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Vaccination; Vaccines, Synthetic --administration and dosage--AD; Vaccines, Synthetic--immunology--IM

CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Antigens, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (Bacterial Proteins); 0 (Bacterial Toxins); 0 (Bacterial Vaccines); 0 (Carrier Proteins); 0 (Enterotoxins); 0 (Escherichia coli Proteins); 0 (Gangliosides); 0 (Recombinant Fusion Proteins); 0 (Vaccines, Synthetic); 0 (enterotoxin LT); 0 (streptococcal M protein)

Record Date Created: 19950505

Record Date Completed: 19950505

19/9/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08989559 PMID: 1718873

Mapping T-cell epitopes in group A streptococcal type 5 M protein.

Robinson J H; Atherton M C; Goodacre J A; Pinkney M; Weightman H; Kehoe M A

Department of Immunology, Medical School, University of Newcastle upon Tyne, United Kingdom.

Infection and immunity (UNITED STATES) Dec 1991, 59 (12) p4324-31, ISSN 0019-9567--Print Journal Code: 0246127

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Group A streptococcal cell surface M proteins elicit highly protective, serotype-specific opsonic antibodies and many serotypes also elicit host cross-reactive antibodies, which may contribute to the pathogenesis of poststreptococcal autoimmune disease. To date, studies aimed at designing safe (non-host-cross-reactive, defined-epitope) M vaccines have focused almost exclusively on antibody epitopes. Here we identify T-cell epitopes recognized by T cells from BALB/c, C57BL/6, and CBA/Ca mice immunized with purified, recombinant serotype 5 M protein (rM5). The responses of rM5-specific, major histocompatibility complex class II-restricted, T-cell clones to synthetic peptides representing most of the M5 sequence identified at least 13 distinct T-cell recognition sites, including sites

recognized by more than one major histocompatibility complex haplotype of mice. Although none of these sites appeared to be strongly immunodominant, an N-terminal peptide, sM5[1-35], was recognized by lymph node T cells of rM5-immunized mice and by a larger proportion of rM5-specific T-cell clones than any other individual peptide. The fine specificity of these clones was mapped with subpeptides to a single site at or overlapping the sequence ELENHDL at residues 21 to 27, which is in close proximity to previously mapped protective antibody epitopes. Other T-cell recognition sites are distributed throughout the M protein and include several in the highly conserved C-terminal region of the molecule. One of these C-terminal sites, located within residues 300 to 319, was recognized by a significant proportion of T-cell clones from two strains of mice. Helper T-cell epitopes located in the C-terminal region of M5 are likely to be widely conserved between different M serotypes and could be particularly useful in designing multivalent, defined-epitope M vaccines.

Descriptors: *Antigens, Bacterial; *Bacterial Outer Membrane Proteins; *Bacterial Proteins--immunology--IM; *Carrier Proteins; *Epitopes--analysis --AN; *Streptococcus pyogenes--immunology--IM; *T-Lymphocytes--immunology --IM; Amino Acid Sequence; Animals; Bacterial Vaccines--immunology--IM; Clone Cells; Lymphocyte Activation; Mice; Mice, Inbred Strains; Molecular Sequence Data; Peptide Fragments--immunology--IM; Protein Conformation; Research Support, Non-U.S. Gov't

CAS Registry No.: 0 (Antigens, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (Bacterial Proteins); 0 (Bacterial Vaccines); 0 (Carrier Proteins); 0 (Epitopes); 0 (Peptide Fragments); 0 (streptococcal M protein)

Record Date Created: 19911224

Record Date Completed: 19911224

19/9/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07000524 PMID: 2422314

Localization of protective epitopes of the amino terminus of type 5 streptococcal M protein.

Dale J B; Beachey E H

Journal of experimental medicine (UNITED STATES) May 1 1986, 163 (5) p1191-202, ISSN 0022-1007--Print Journal Code: 2985109R

Contract/Grant No.: AI-10085; AI; NIAID; AI-13550; AI; NIAID

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We have used a set of overlapping chemically synthesized peptides representing the amino terminus of type 5 streptococcal M protein to localize protective, as opposed to nonprotective and tissue-crossreactive epitopes that might be appropriate for vaccine formulations. Rabbit antisera raised against SM5(1-35) reacted in high titer with pep M5 by ELISA and opsonized type 5 streptococci. None of the antisera crossreacted with human heart tissue or myosin. Antisera against SM5(26-35) reacted with SM5(1-35) and pep M5 but failed to opsonize type 5 streptococci. Particle-phase ELISA indicated that SM5(26-35) antibodies were directed against nonprotective determinants of pep M5 that were not exposed on the surface of viable organisms. Opsonization and ELISA inhibition assays showed that, of the SM5(1-35) antibodies that reacted with M5, all were inhibited by SM5(14-35), whereas none was inhibited by SM5(26-35),

suggesting that the protective epitopes of SM5(1-35) resided between residues 14 and 26. This was confirmed by subsequent chemical synthesis of this region; SM5(14-26) totally inhibited SM5(1-35) antibodies that reacted with pep M5 in ELISA, and completely inhibited opsonization of type 5 streptococci by SM5(1-35) antibodies. SM5(14-26) evoked high titers of type-specific, opsonic antibodies against type 5 streptococci, confirming the protective immunogenicity of this 13-residue peptide of type 5 M protein.

Descriptors: *Antigens, Bacterial--immunology--IM; *Bacterial Outer Membrane Proteins; *Bacterial Proteins--immunology--IM; *Bacterial Vaccines --immunology--IM; *Carrier Proteins; *Streptococcus pyogenes--immunology --IM; Amino Acid Sequence; Antibodies, Bacterial--biosynthesis--BI; Antibody Specificity; Cross Reactions; Epitopes; Peptides --chemical synthesis--CS; Peptides--immunology--IM; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Antigens, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (Bacterial Proteins); 0 (Bacterial Vaccines); 0 (Carrier Proteins); 0 (Epitopes); 0 (Peptides); 0 (streptococcal M protein)

Record Date Created: 19860606

Record Date Completed: 19860606

19/9/8 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0013078193 BIOSIS NO.: 200100250032

Comparison of SM5-1 immunoreactivity with anti-Melan A and anti-tyrosinase antibodies in melanoma lesions

AUTHOR: Reinke S (Reprint); Koeniger P; Chen Y W; Herberth G; Audring H; Sterry W; Trefzer U

AUTHOR ADDRESS: Department of Dermatology, Humboldt-University, Charite, Berlin, Germany**Germany

JOURNAL: Archives of Dermatological Research 293 (1-2): p69 February, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: XXVIII Annual Meeting of the Arbeitsgemeinschaft Dermatologische Forschung in Cooperation with the German Dermatological Society Munich, Germany February 15-17, 2001; 20010215

SPONSOR: Deutsche Dermatologische Gesellschaft

ISSN: 0340-3696

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Oncology--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--patient

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: melanoma--neoplastic disease, immunodiagnosis

MESH TERMS: Melanoma (MeSH)

CHEMICALS & BIOCHEMICALS: SM-5-1 antibody--comparative tumor lesion immunoreactivity, diagnostic marker, immunohistological staining pattern; anti-Melan-A antibody--comparative tumor lesion immunoreactivity, diagnostic marker, immunohistological staining pattern; antityrosinase antibody--comparative tumor lesion immunoreactivity, diagnostic marker, immunohistological staining

pattern
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
24004 Neoplasms - Pathology, clinical aspects and systemic effects
00520 General biology - Symposia, transactions and proceedings
BIOSYSTEMATIC CODES:
86215 Hominidae

19/9/9 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011663512 BIOSIS NO.: 199800457759
A melanoma associated fibronectin variant characterized by monoclonal antibody SM5-1
AUTHOR: Chen Y; Guo Y J; Herberth G; Adrian K; Siegel P; Audring H; Hansen-Hagge T; Sterry W; Trefzer U
AUTHOR ADDRESS: Dep. Dermatol., Charite, Humboldt Univ., 10115 Berlin, Germany**Germany
JOURNAL: Journal of Molecular Medicine (Berlin) 76 (6): pB11 May, 1998 1998
MEDIUM: print
CONFERENCE/MEETING: 2nd Congress of Molecular Medicine Berlin, Germany May 6-9, 1998; 19980506
ISSN: 0946-2716
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Immune System--Chemical Coordination and Homeostasis; Tumor Biology
BIOSYSTEMATIC NAMES: Animalia--Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: SMMUneg (Animalia)--melanoma cells; SMMUpos (Animalia)--melanoma cells; human (Hominidae); mouse (Muridae)--model
COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates
DISEASES: melanoma--neoplastic disease
MESH TERMS: Melanoma (MeSH)
CHEMICALS & BIOCHEMICALS: fibronectin; monoclonal antibody SM5-1
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
24002 Neoplasms - General
02502 Cytology - General
10060 Biochemistry studies - General
13002 Metabolism - General metabolism and metabolic pathways
34502 Immunology - General and methods
00520 General biology - Symposia, transactions and proceedings
BIOSYSTEMATIC CODES:
33000 Animalia
86215 Hominidae
86375 Muridae

19/9/10 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011498368 BIOSIS NO.: 199800292615
SM5-1: A new monoclonal antibody which is highly sensitive and specific for melanocytic tumors
AUTHOR: Trefzer Uwe; Herberth Gunda; Chen Ying-Wen; Rietz Nadine; Audring Heike; Siegel Petra; Adrian Karin; Winter Helmut; Guo Ya-Jun; Sterry Wolfram
AUTHOR ADDRESS: Dep. Dermatology, Humbodlt-Univ., Chartie, Berlin, Germany **Germany
JOURNAL: Journal of Dermatological Science 16 (SUPPL. 1): pS110 March, 1998 1998
MEDIUM: print
CONFERENCE/MEETING: Third Joint Meeting of the European Society for Dermatological Research, Japanese Society for Investigative Dermatology, Society for Investigative Dermatology Cologne, Germany May 7-10, 1998; 19980507
SPONSOR: European Society for Dermatological Research
Japanese Society for Investigative Dermatology
Society for Investigative Dermatology
ISSN: 0923-1811
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Integumentary System--Chemical Coordination and Homeostasis
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae); mouse (Muridae)
COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates
DISEASES: melanocytic tumor--neoplastic disease
CHEMICALS & BIOCHEMICALS: SM5-1--monoclonal antibody
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
18501 Integumentary system - General and methods
24002 Neoplasms - General
00520 General biology - Symposia, transactions and proceedings
BIOSYSTEMATIC CODES:
86215 Hominidae
86375 Muridae

19/9/11 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 Inst for Sci Info. All rts. reserv.

12367260 Genuine Article#: 756LU Number of References: 0
Title: Monoclonal antibody SM5-1 can inhibit tumor cells' growth and induce caspase-10 related apoptosis.
Author(s): Dai JX; Jin J; Yang SL; Ma J; Qian WZ; Wang H; Guo YJ
Corporate Source: Eppley Inst Res Canc,Omaha//NE/; Shanghai Int Joint Canc Inst,Shanghai//Peoples R China/
Journal: CLINICAL CANCER RESEARCH, 2003, V9, N16,2,S (DEC 1), P6206S-6207S
ISSN: 1078-0432 Publication date: 20031201
Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA
Language: English Document Type: MEETING ABSTRACT
Geographic Location: USA; Peoples R China
Journal Subject Category: ONCOLOGY
?

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Set     Items   Description
S1       5254   (FLT3 (W) LIGAND)
S2       1166   (CHIMERA OR CHIMAERA) AND (FUSION (W) PROTEIN)
S3          8   S1 AND S2
S4          4   RD S3  (unique items)
S5         80   (S1 AND CHIMERA)
S6         52   RD S5  (unique items)
S7      39485   (APOPTOSIS AND ANTIBODY)
S8          1   S7 AND S6
S9        121   (S1 AND (FUSION (W) PROTEIN))
S10        60   RD S9  (unique items)
S11        11   (S10 AND APOPTOSIS)
S12        11   RD S11  (unique items)
S13         0   (P230 (W) ANTIBODY)
S14         0   SM5 (W) ANTIBODY
S15       396   (P (W) 230)
S16         2   S15 AND ANTIBODY
S17         2   RD S16  (unique items)
S18        30   (SM5 (W) 1)
S19        11   RD S18  (unique items)
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 NEWS  7  MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                  USPATFULL/USPAT2
 NEWS  9  MAY 30  The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02  The first reclassification of IPC codes now complete in
                  INPADOC
 NEWS 11  JUN 26  TULSA/TULSA2 reloaded and enhanced with new search and
                  and display fields
 NEWS 12  JUN 28  Price changes in full-text patent databases EPFULL and PCTFULL

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                  CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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                  http://download.cas.org/express/v8.0-Discover/

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=> s ((flt (n) 3) or (flt3) and (chimera or chimaera))
L1 1113 ((FLT (N) 3) OR (FLT3) AND (CHIMERA OR CHIMAERA))

=> s l1 and fusion)
UNMATCHED RIGHT PARENTHESIS 'FUSION)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l1 and fusion
L2 78 L1 AND FUSION

=> s l1 and Flex
L3 6 L1 AND FLEX

=> duplicate remove l3
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L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> d l4 bib abs 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2006:446989 CAPLUS
DN 144:481584
TI Augmenting the immunogenicity of DNA vaccines: Role of plasmid-encoded Flt-3 ligand, as a molecular adjuvant in genetic vaccination
AU Nayak, Bishnu P.; Sailaja, Gangadhara; Jabbar, Abdul M.
CS Emory Vaccine Center, Department of Microbiology and Immunology, Emory University School of Medicine, Emory University, Atlanta, GA, 30329, USA
SO Virology (2006), 348(2), 277-288
CODEN: VIRLAX; ISSN: 0042-6822
PB Elsevier
DT Journal
LA English
AB In this study, the authors have taken advantage of the unique property of a potent dendritic cell (DC) growth factor, Flt-3 ligand (FL), which could act as a vaccine adjuvant. Accordingly, a single injection of plasmid DNA coding for soluble FL (FLex) was shown to induce large nos. of DCs in various tissue compartments and was critical for generating high frequencies of antigen-specific (HIV gp120 and LCMV NP) immune responses in mice. Interestingly, this enhanced level of immune response is strictly dependent on the co-delivery (i.m.) of the DNA vaccines and hFLex DNA to mice harboring large nos. of DCs. The high frequencies of antigen-specific CD8+ T cells were largely associated with the expansion phase of DCs in vivo. However, DC expansion and immune enhancement have not reciprocally maintained a linear correlation, suggesting that other factors, cytokines/chemokines, which have the potential to modulate the microenvironment of DCs, could influence

immunol. outcome in this vaccination modality.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2003:129250 CAPLUS
DN 138:236497
TI Long-Term Maintenance of gp120-Specific Immune Responses by Genetic Vaccination with the HIV-1 Envelope Genes Linked to the Gene Encoding Flt-3 Ligand
AU Sailaja, Gangadhara; Husain, Sajid; Nayak, Bishnu P.; Jabbar, Abdul M.
CS Emory University School of Medicine, Department of Microbiology and Immunology, Emory Vaccine Center at Yerkes, Atlanta, GA, 30329, USA
SO Journal of Immunology (2003), 170(5), 2496-2507
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB DNA vaccines target dendritic cells (DC) to induce antigen-specific immune responses in animals. Potent HIV-specific immunity could be achieved by efficient priming of the immune system by DNA vaccines. The authors investigated a novel DNA vaccine approach based on the role of growth factors in DC expansion and differentiation. To this end, they constructed chimeric genes encoding the HIV envelope glycoproteins phys. linked to the extracellular domain of Fms-like tyrosine kinase receptor-3 ligand (FLex; a DC growth factor; both mouse (m)FLex and human (h)FLex). These chimeric gene constructs synthesized biol. active, oligomeric FLex:gp120 fusion proteins and induced DC expansion (CD11c+CD11b+) when injected i.v. into mice. This DC expansion is comparable to that achieved by FLex DNA encoding native FLex protein. When delivered i.m. as DNA vaccines, hFLex:gp120 induced high frequencies of gp120-specific CD8+ T cells in the presence or absence of FLex DNA-induced DC expansion, but gp120 and mFLex:gp120 elicited only low to moderate levels of Ag-specific CD8+ T cells. In contrast, mFLex:gp120 induced high levels of anti-gp120 Abs under identical conditions of DNA vaccination. However, the Ab levels in mice immunized with DNA vaccines encoding hFLex:gp120 and gp120 proteins were low without DC expansion, but reached high levels comparable to that elicited by mFLex:gp120 only after the second boost in the presence of DC expansion. Importantly, the gp120-specific CD8+ T cells persisted at high frequency for 114 days (16 wk) after a booster injection. These expts. provide insight into the importance of modulating DC function in vivo for effective genetic vaccination in animals.
RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s (flex and (fusion or chimera or chimaera))
L5 44 (FLEX AND (FUSION OR CHIMERA OR CHIMAERA))

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
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L6 34 DUPLICATE REMOVE L5 (10 DUPLICATES REMOVED)

=> d l6 bib abs 1-34

L6 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:510742 CAPLUS
DN 145:2128
TI Gene trap cassettes for random and targeted conditional gene inactivation
IN Von Melchner, Harald; Schnuetgen, Frank; Wurst, Wolfgang; Ruiz, Patricia; De-Zolt, Silke; Floss, Thomas; Hansen, Jens

PA Frankgen Biotechnologie A.-G., Germany; GSF Forschungszentrum fuer Umwelt und Gesundheit G.m.b.H.; MPG Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V.

SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006056617	A1	20060601	WO 2005-EP56282	20051128
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	EP 1662005	A1	20060531	EP 2004-28194	20041126
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRAI	EP 2004-28194	A	20041126		
	EP 2005-103092	A	20050418		

AB The present invention provides for a new type of gene trap cassettes, which can induce conditional mutations. The cassettes rely on directional site-specific recombination systems, which can repair and re-induce gene trap mutations when activated in succession. After the gene trap cassettes are inserted into the genome of the target organism, mutations can be activated at a particular time and place in somatic cells. Moreover, the invention relates to the use of said cell for identification and/or isolation of genes and for the creation of transgenic organisms to study gene function at various developmental stages, including the adult, as well as for the creation of animal models of human disease useful for in vivo drug target validation. In conclusion, the present invention provides a process which enables a temporally and/or spatially restricted inactivation of all genes that constitute a living organism. Two gene trap vectors were designed for large scale conditional mutagenesis in ES cells. The first vector FlipRosaβgeo contains a classic splice acceptor (SA) - β-galactosidase/neomycintransferase fusion gene (βgeo) - polyadenylation sequence (pA) cassette inserted into the backbone of a promoter- and enhancerless Moloney murine leukemia virus in inverse transcriptional orientation relative to the virus [Friedrich, G. & Soriano, P. (1991) Genes Dev. 5, 1513-1523]. The second vector FlipRosaCeo is similar to FlipRosaβgeo except that SAβgeo has been exchanged with Ceo, which is an in frame fusion between the human CD2 cell surface receptor- and the neomycin resistance genes (Gebauer, M. et al., Genome Res 11, 1871-7 (2001)). Unlike βgeo, Ceo does not require an extra splice acceptor site for trapping as it contains a powerful cryptic 5' splice site close to its 5' end. The mechanism relies on two site-specific recombination systems (FLPe/frt; Cre/loxP), which enable gene trap cassette inversions from the sense, coding strand of a trapped gene to the antisense, noncoding strand and back. As a result, the gene trap vectors allow (i) high throughput selection of gene trap lines using G418, [ii] inactivation of gene trap mutations prior to ES cell line conversion into mice by blastocyst injection, and (iii) reactivation of the mutations at prespecified times and in selected tissues of the resulting mice.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1082020 CAPLUS
DN 142:62606
TI Protein and nucleotide sequences and application of anti-tumor bifunctional fusion proteins
IN Ma, Jing; Guo, Yajun
PA USA
SO U.S. Pat. Appl. Publ., 158 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004254108	A1	20041216	US 2003-723003	20031126
	AU 2004252465	A1	20050106	AU 2004-252465	20040604
	CA 2528595	AA	20050106	CA 2004-2528595	20040604
	WO 2005001048	A2	20050106	WO 2004-US17765	20040604
	WO 2005001048	A3	20050616		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1633398	A2	20060315	EP 2004-776301	20040604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2005232931	A1	20051020	US 2004-4639	20041202
PRAI	CN 2003-129290	A	20030613		
	CN 2003-10119930	A	20031125		
	US 2003-723003	A	20031126		
	TW 2003-92133577	A	20031128		
	WO 2004-US17765	W	20040604		

AB Provided herein is a chimeric protein, which chimeric protein comprises a Flt3 ligand, or a biol. active fragment thereof, and a proteinuous or peptidyl tumoricidal agent, and uses thereof, particularly in the treatment of malignancy.

L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:307583 CAPLUS
DN 140:305369
TI Automobile interior skin materials having smooth surface and soft touch and their manufacture
IN Kataoka, Toshihiro
PA Kureha Tec K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2004114815	A2	20040415	JP 2002-280124	20020926
PRAI	JP 2002-280124		20020926		

AB The materials comprise needle-punched and fused nonwovens of high-m.p. fiber/hot-melt fiber blends satisfying fraction of the latter fiber 5-50%,

and satisfy compression modulus 0.6-1.2 g/mm3 per 100-g/mm2, flex rigidity ≤200 mm, and friction coefficient ≤0.45. The materials are manufactured by passing hot air through needle-punched nonwovens and pressing rollers on the nonwovens. The high-m.p. fibers may be polyester fibers, polypropylene fibers, polyamide fibers, etc. Thus, a nonwoven of 80:20 (%) polyester fiber (m.p. 260°)/composite polyester fiber (m.p. of lower component; 110°) was needle-punched, passed through hot air, and pressed with hot rolls (roll temperature 70°) to give a product showing flex rigidity 139 mm, compression modulus 1.15 g/mm3,and friction coefficient 0.40.

L6 ANSWER 4 OF 34 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-06297 BIOTECHDS
TI New CH1 deleted mimetibody polypeptide and nucleic acid, useful for diagnosing, preventing or treating cardiovascular, dermatologic, endocrine, gastrointestinal, gynecologic, infectious, neurologic and nutritional disorders;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy
AU HEAVNER G A; KNIGHT D M; GHRAYEB J; SCALLON B J; NESSPOR T C; KUTOLOSKI K A
PA CENTOCOR INC
PI WO 2004002424 8 Jan 2004
AI WO 2003-US20495 30 Jun 2003
PRAI US 2002-412144 19 Sep 2002; US 2002-392431 28 Jun 2002
DT Patent
LA English
OS WPI: 2004-082872 [08]
AN 2004-06297 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - At least one CH1 deleted mimetibody nucleic acid (I) comprises at least one polynucleotide encoding a 269 or 266 amino acid sequence (SEQ ID NO: 1112 or 1113), given in the specification, or its complement, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) at least one CH1 deleted mimetibody nucleic acid, comprising at least one polynucleotide encoding a polypeptide with formula (I); (2) at least one CH1 deleted mimetibody polypeptide, comprising all of the contiguous amino acids of SEQ ID NO: 1112 or 1113; (3) at least one CH1 deleted mimetibody polypeptide, comprising a polypeptide with Formula (I); (4) a CH1 deleted mimetibody antibody, comprising a monoclonal or polyclonal antibody, fusion protein, or its fragment, that specifically binds at least one CH1 deleted mimetibody polypeptide of (2) or (3); (5) a CH1 deleted mimetibody nucleic acid encoding at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody; (6) a CH1 deleted mimetibody vector comprising at least one isolated nucleic acid cited above or encoding, or complementary to such nucleic acid encoding, a CH1 deleted mimetibody polypeptide; (7) a CH1 deleted mimetibody host cell comprising an isolated nucleic acid of (6); (8) producing at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody, comprising translating a nucleic acid of (5) under conditions in vitro, in vivo or in situ, so that the CH1 deleted mimetibody or antibody is expressed in detectable or recoverable amounts; (9) a composition comprising at least one CH1 deleted mimetibody nucleic acid, CH1 deleted mimetibody polypeptide, or CH1 deleted mimetibody antibody; (10) diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal, comprising contacting or administering a composition comprising an effective amount of a composition of (9), with, or to, the cell, tissue, organ or animal; (11) a device, comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, wherein the device is suitable for contacting or administering the at least one of the CH1 deleted mimetibody polypeptide, antibody or nucleic acid, by at least one mode selected from parenteral,

subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal; (12) an article of manufacture for human pharmaceutical or diagnostic use, comprising packaging material and a container comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (13) producing at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, comprising providing at least one host cell, transgenic animal, transgenic plant, plant cell capable of expressing in detectable or recoverable amounts the polypeptide, antibody or nucleic acid; and (14) at least one CH1 deleted mimetibody polypeptide, antibody or nucleic acid, produced by the method of (13). (V1(n)-Pep-Flex(n)-V2(n)-pHinge(n)-CH2(n)-CH3(n))(m) (I) V1 = at least one portion of an N-terminus of an immunoglobulin variable region or an Asn-terminal portion of a human variable region or Gln Ile Gln; Pep = at least one bioactive peptide from any of 42 or 609 amino acid sequences (SEQ ID NO: 1-42 or 501-1110), given in the specification; Flex = a polypeptide that provides structural flexibility by allowing the mimetibody to have alternative orientations and binding properties; V2 = at least one portion of a C-terminus of an immunoglobulin variable region or SEQ ID NO: 1126; pHinge = at least a portion of an immunoglobulin variable hinge region or SEQ ID NO: 1120; CH2 = at least a portion of an immunoglobulin CH2 constant region; CH3 = at least a portion of an immunoglobulin CH3 constant region; and n and m = an integer 1-10; In formula (I) of (3): V1 = Gln-Ile-Gln; Pep = at least one bioactive peptide selected from any of 42 amino acid sequences given in the specification (SEQ ID NOS:1-42); Flex = Gly Gly Gly Ser; V2 = SEQ ID NO: 1126; pHinge = SEQ ID NO: 1120; CH2 = SEQ ID NO: 1121 or 1124; CH3 = SEQ ID NO:1122 or 1125; and n and m = an integer 1-10.

BIOTECHNOLOGY - Preferred Polypeptide: The polypeptide has at least one activity of at least one Pep polypeptide. Preferred Composition: The composition further comprises at least one carrier or diluent, and at least one compound, composition or polypeptide selected from at least one of a detectable label or reporter, a tumor necrosis factor (TNF) antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug, a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a form of at least one selected from a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or a powder. Preferred Method: Diagnosing or treating a CH1 deleted mimetibody ligand related condition further comprises administering, prior, concurrently or after the contacting or administering, at least one composition of at least one compound, composition or polypeptide selected from at least one of a detectable label or reporter, a TNF antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug, a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist.

ACTIVITY - Osteopathic; Cardiovascular-Gen.; Dermatological-Gen.; Auditory; Endocrine-Gen.; Gastrointestinal-Gen.; Gynecological-Gen.; Hepatotropic; Hemostatic; Immunomodulator; Antiallergic; Muscular-Gen.; Cytostatic; Antiinflammatory; Neuroleptic; Ophthalmological;

Nephrotropic; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - TNF-Modulator; Cytokine-Agonist.

USE - The methods and compositions of the present invention are useful for the diagnosis, prevention and/or treatment of diseases or conditions associated with aberrant expression or activity of the CH1 deleted mimetibody, such as a bone or joint, cardiovascular, dental or oral, dermatologic, ear, nose or throat, endocrine, metabolic, gastrointestinal, gynecologic, hepatic, obstetric, hematologic, immunologic, allergic, infectious, musculoskeletal, oncologic, neurologic, nutritional, ophthalmologic, pediatric, psychiatric, renal or pulmonary disorders.

ADMINISTRATION - The effective amount of the pharmaceutical composition is 0.001-50 mg of CH1 deleted mimetibody antibody, 0.000001-500 mg of the CH1 deleted mimetibody, or 0.0001-100 microg of the CH1 deleted mimetibody nucleic acid per kilogram of the cells, tissue, organ or animal. The contacting or the administrating is by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal. (All claimed.)

EXAMPLE - Experimental protocols are described but no results given. (123 pages)

L6 ANSWER 5 OF 34 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-06296 BIOTECHDS
TI New CH1-deleted mimetibody polypeptides and nucleic acids, useful for modulating, treating, alleviating, preventing an immune, cardiovascular, or neurodegenerative disease or disorder, anemia, cancer, or infectious diseases;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy
AU HEAVNER G A; KNIGHT D M; GHRAYEB J; SCALLON B J; NESSPOR T C; KUTOLOSKI K A
PA CENTOCOR INC
PI WO 2004002417 8 Jan 2004
AI WO 2003-US20347 27 Jun 2003
PRAI US 2002-392431 28 Jun 2002; US 2002-392431 28 Jun 2002
DT Patent
LA English
OS WPI: 2004-082870 [08]
AN 2004-06296 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A CH1-deleted mimetibody nucleic acid comprising at least one polynucleotide encoding a polypeptide having formula (I), is new.

DETAILED DESCRIPTION - A CH1-deleted mimetibody nucleic acid comprising at least one polynucleotide encoding a polypeptide having formula (I), is new. ((V1)(n)-Pep(n)-Flex(n)-V2(n)-pHinge(n)-CH2(n)-CH3(n))(m) (I). V1 = at least one portion of an N-terminus of an immunoglobulin (Ig) variable region; Pep = at least one bioactive peptide; Flex = a polypeptide that provides structural flexibility by allowing the mimetibody to have alternative orientations and binding properties; V2 = at least one portion of a C-terminus of an Ig variable region; pHinge = at least a portion of an Ig variable hinge region; CH2 = at least a portion of an Ig CH2 constant region; CH3 = at least a portion of an Ig CH3 constant region; and n and m = an integer 1-10. INDEPENDENT CLAIMS are also included for: (1) a CH1 deleted mimetibody antibody comprising a monoclonal or polyclonal antibody, fusion protein, or its fragment that specifically binds at least

one CH1 deleted mimetibody polypeptide; (2) a CH1 deleted mimetibody nucleic acid encoding at least one CH1 deleted mimetibody polypeptide or the CH1 deleted mimetibody antibody;(3) a CH1 deleted mimetibody vector or host cell comprising at least one isolated nucleic acid of (2); (4) producing at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody by translating a nucleic acid of (2) in vitro, in vivo or in situ, so that the CH1 deleted mimetibody or antibody is expressed in detectable or recoverable amounts; (5) a composition comprising at least one of the CH1 deleted mimetibody nucleic acid, polypeptide, or antibody; (6) diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal; (7) a device comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, and suitable for contacting or administering the CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (8) an article of manufacture for human pharmaceutical or diagnostic use, comprising a packaging material and a container comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (9) producing at least one isolated CH1 deleted mimetibody; and (10) at least one CH1 deleted mimetibody polypeptide, antibody or nucleic acid, produced from the method.

WIDER DISCLOSURE - (1) vectors comprising the CH1-deleted mimetibody nucleic acid; and (2) host cells genetically engineered with the recombinant vectors.

BIOTECHNOLOGY - Preferred Nucleic Acid: The Pep is a bioactive peptide selected from 1067 sequences (SEQ ID NOS: 43-1110) given in the specification. The CH1 deleted mimetibody polypeptide has at least one activity of at least one Pep polypeptide. Preferred Composition: The composition further comprises at least one pharmaceutical carrier or diluent, and at least one composition comprising one compound, composition or polypeptide selected from a detectable label or reporter, a tumor necrosis factor (TNF) antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or powder form. Preparation: The CH1-deleted mimetibody nucleic acid may be prepared by recombinant, synthetic or purification techniques. Preferred Method: Diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal, comprises contacting or administering a composition comprising at least one CH1 deleted mimetibody nucleic acid, polypeptide or antibody with or to the cell, tissue, organ or animal. The amount of CH1 deleted antibody administered is 0.001-50, 0.000001-500 mg of the CH1 deleted mimetibody, or 0.0001-100 microg of the CH1 deleted mimetibody nucleic acid per kilogram of the cells, tissue, organ or animal. Contacting or administration is by parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal means. The method further comprises administering prior, concurrently or after administration, at least one composition comprising at least one compound or polypeptide selected from a detectable label or reporter, a TNF antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an

antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or powder form. Producing at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid comprises providing at least one host cell, transgenic animal, transgenic plant, plant cell capable of expressing in detectable or recoverable amounts the polypeptide, antibody or nucleic acid. Preferred Article: The container is a component of a parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal delivery device or system.

ACTIVITY - Immunosuppressive; Cardiovascular; Cardiant; Hypotensive; Neuroprotective; Nootropic; Antibacterial; Virucide; Fungicide. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The CH1-deleted mimetibody is useful for diagnosing or treating a disease condition in a cell, tissue, organ or animal, specifically for modulating, treating, alleviating, preventing the incidence or reducing the symptoms of an immune, cardiovascular (e.g. arrhythmia, hypertension or heart failure), or neurodegenerative (e.g. multiple sclerosis, dementia or Alzheimer's disease) diseases or disorders, anemia, cancerous conditions, or infectious diseases (e.g. bacterial, viral or fungal infection).

ADMINISTRATION - Administration can be through parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal means (claimed) at a dose of 0.0001-500 mg/kg per single or multiple administration.

EXAMPLE - Experimental protocols are described but no results are given.(129 pages)

L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2004:161217 CAPLUS
DN 140:403122
TI ADAM family protein Mde10 is essential for development of spore envelopes in the fission yeast Schizosaccharomyces pombe
AU Nakamura, Tomohiro; Abe, Hiroko; Hirata, Aiko; Shimoda, Chikashi
CS Faculty of Intellectual Property, Osaka Institute of Technology, Osaka, 535-8585, Japan
SO Eukaryotic Cell (2004), 3(1), 27-39
CODEN: ECUEA2; ISSN: 1535-9778
PB American Society for Microbiology
DT Journal
LA English
AB We report the identification of Schizosaccharomyces pombe mde10+ as a gene possessing a FLEX element, which forms a binding site for the meiosis-specific transcription factor Mei4. In fact, mde10+ is transcribed only in diploid cells that are induced to meiosis in a Mei4-dependent manner. Western blot anal. indicated that the epitope-tagged Mde10 protein accumulates transiently during meiosis and then rapidly decreases. Mde10 is a multidomain protein containing a

metalloprotease catalytic domain, a disintegrin domain, a cysteine-rich domain, and membrane-spanning regions, all of which are shared by members of the mammalian ADAM family. A fusion protein of Mde10 and green fluorescent protein localized to the endoplasmic reticulum during meiosis and was located at the peripheral region of spores at the end of meiosis. An mde10Δ deletion mutant showed no apparent defects in meiosis, sporulation, or spore germination. However, the mutant spores exhibited an aberrant surface appearance, in which the ragged outer spore wall was lost to a large extent. Furthermore, mde10Δ spores were found to be less tolerant to ethanol and di-Et ether than were wild-type spores. The mutagenic replacement of the conserved glutamic acid in the putative protease active site with an alanine residue did not affect the surface morphol. or the resistance of spores to environmental stress. Our observations indicate that Mde10 is important in the development of the spore envelope, although this function of Mde10 seems to be independent of its metalloprotease activity.

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2003:129250 CAPLUS
DN 138:236497
TI Long-Term Maintenance of gp120-Specific Immune Responses by Genetic Vaccination with the HIV-1 Envelope Genes Linked to the Gene Encoding Flt-3 Ligand
AU Sailaja, Gangadhara; Husain, Sajid; Nayak, Bishnu P.; Jabbar, Abdul M.
CS Emory University School of Medicine, Department of Microbiology and Immunology, Emory Vaccine Center at Yerkes, Atlanta, GA, 30329, USA
SO Journal of Immunology (2003), 170(5), 2496-2507
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB DNA vaccines target dendritic cells (DC) to induce antigen-specific immune responses in animals. Potent HIV-specific immunity could be achieved by efficient priming of the immune system by DNA vaccines. The authors investigated a novel DNA vaccine approach based on the role of growth factors in DC expansion and differentiation. To this end, they constructed chimeric genes encoding the HIV envelope glycoproteins phys. linked to the extracellular domain of Fms-like tyrosine kinase receptor-3 ligand (FLex; a DC growth factor; both mouse (m)FLex and human (h)FLex). These chimeric gene constructs synthesized biol. active, oligomeric FLex:gp120 fusion proteins and induced DC expansion (CD11c+CD11b+) when injected i.v. into mice. This DC expansion is comparable to that achieved by FLex DNA encoding native FLex protein. When delivered i.m. as DNA vaccines, hFLex:gp120 induced high frequencies of gp120-specific CD8+ T cells in the presence or absence of FLex DNA-induced DC expansion, but gp120 and mFLex:gp120 elicited only low to moderate levels of Ag-specific CD8+ T cells. In contrast, mFLex:gp120 induced high levels of anti-gp120 Abs under identical conditions of DNA vaccination. However, the Ab levels in mice immunized with DNA vaccines encoding hFLex:gp120 and gp120 proteins were low without DC expansion, but reached high levels comparable to that elicited by mFLex:gp120 only after the second boost in the presence of DC expansion. Importantly, the gp120-specific CD8+ T cells persisted at high frequency for 114 days (16 wk) after a booster injection. These expts. provide insight into the importance of modulating DC function in vivo for effective genetic vaccination in animals.

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:180837 CAPLUS
TI Spinal implant device

IN Nolan, Wesley A.
PA USA
SO PCT Int. Appl.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002019952	A1	20020314	WO 2000-US24568	20000908
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000073558	A5	20020322	AU 2000-73558	20000908
EP 1427358	A1	20040616	EP 2000-961636	20000908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI WO 2000-US24568	A	20000908		

AB A dynamic fusion device for facilitating arthrodesis in a disk space between adjacent vertebrae that includes a body and an engaging member. The body extends along a longitudinal axis having a first portion and two or more legs depending from the first portion. The legs are laterally spaced apart from each other and define a second end of the body spaced opposite the first end. The legs define an engaging member receiving cavity. An engaging member, such as a disk, is secured to the body and receiving within the engaging member receiving cavity, wherein the engaging member is secured to the body only by engagement of the engaging member with the legs. During installation, the engaging member causes the legs to flex.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:194045 CAPLUS
DN 135:46868
TI Miscibility and cocrystallization behavior of two melt-processable random copolymers of tetrafluoroethylene and perfluoroalkylvinyl ether
AU Lee, J.-C.; Namura, S.; Kondo, S.; Abe, A.
CS Technical Center, 3600 Miho, Dupont-Mitsui Fluorochemicals Co. Ltd., Shimizu, Shizuoka, 424-8631, Japan
SO Polymer (2001), 42(12), 5453-5461
CODEN: POLMAG; ISSN: 0032-3861
PB Elsevier Science Ltd.
DT Journal
LA English
AB Miscibility, crystallization behavior, and mech. properties of blends made from melt-processable perfluoropolymers of poly(tetrafluoroethylene-co-perfluoropropylvinyl ether) (PFA) and poly(tetrafluoroethylene-co-perfluoroethylvinyl ether) (EFA) were examined by differential scanning calorimetry (DSC) and dynamic mech. anal. (DMA). PFA and EFA (PEVE comonomer:5.7 wt%) blends cocrystallize regardless of crystallization speed and blending method. On the other hand, PFA/EFA blends that contain EFA with high PEVE comonomer content (PEVE:13.3 wt%) formed segregated crystals. However, these blends [PFA/EFA (PEVE:13.3%)] showed a composition dependent single α-relaxation temperature which suggests that they are miscible in the amorphous phase. Therefore, it is concluded that PFA/EFA blends are miscible in the amorphous or molten state, they form segregated crystals

during crystallization In contrast, EFA containing low PEVE content form cocrystals
with PFA from the melt. Measuring the flex life (folding endurance) of the blends revealed that only 20% EFA (PEVE: 13.3%) is required to increase the flex life of neat PFA by four times.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:825689 CAPLUS
DN 137:74080
TI Construction of a fusion gene expression library screening in vivo-induced genes in Shigella flexneri 2a
AU Shi, Zhaoxing; Wang, Hengliang; Feng, Erling; Yao, Xiao; Liao, Xiang; Huang, Liuyu; Su, Guofu; Huang, Cuifen
CS Institute of Biotechnology, Academy of Military Medical Sciences, Beijing, 100071, Peop. Rep. China
SO Xibao Yu Fenzi Mianyixue Zazhi (2001), 17(5), 432-433
CODEN: XFMZFM; ISSN: 1007-8738
PB Disi Junyi Daxue
DT Journal
LA Chinese
AB A fusion gene expression library screening in vivo-induced genes in Flex shigella was constructed. Based on the suicide vector pGP704, a new screening in vivo- induced genes vector pGPcat was constructed with chloramphenicol acetyltransferase(cat) gene as a report gene. The random Shigella flexneri 2a DNA fragments (0.6-1kb), obtained by partial Sau3A1 restriction digestion, were subcloned into the unique Bg1 II site of pGPcat, 5' to the promoterless reporter gene. And the fusion gene library was constructed. The fusion gene expression library was obtained by mating into Shigella flexneri strain 2457T. 3.2% Cmr strains were obtained by screening in vitro with chloramphenicol as the selectable marker. The expression library is suitable for screening in vivo- induced genes of Shigella flexneri 2a.

L6 ANSWER 11 OF 34 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2001:32514653 BIOTECHNO
TI Regression of human mammary adenocarcinoma by systemic administration of a recombinant gene encoding the hFlex-TRAIL fusion protein
AU Wu X.; He Y.; Falo L.D. Jr.; Hui K.M.; Huang L.
CS Dr. L. Huang, Center for Pharmacogenetics, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15216, United States.
E-mail: Huangl@msx.upmc.edu
SO Molecular Therapy, (2001), 3/3 (368-374), 35 reference(s)
CODEN: MTOHCK ISSN: 1525-0016
DT Journal; Article
CY United States
LA English
SL English
AB The tumor necrosis factor (TNF)-related apoptosis-inducing ligand, TRAIL, is a new member of the TNF family. It can specifically induce apoptosis in a variety of human tumors. To investigate the possibility of employing the TRAIL gene for systemic cancer therapy, we constructed a recombinant gene encoding the soluble form of the human Flt3L gene (hFlex) at the 5' end and the human TRAIL gene at the 3' end. Such design allows the TRAIL gene product to be secreted into the body circulation. We have also demonstrated that the addition of an isoleucine zipper to the N-terminal of TRAIL greatly enhanced the trimerization of the fusion protein and dramatically increased its anti-tumor activity. The fusion protein reached the level of 16-38 μg/ml in the serum after a single administration of the recombinant gene by hydrodynamic-based gene delivery in mice. A high level of the fusion protein correlated with the regression of a human breast tumor established in SCID mice. No apparent toxicity was observed in the

SCID mouse model. In addition, the fusion protein caused an expansion of the dendritic cell population in the C57BL/6 recipient mice, indicating that the hFlex component of the fusion protein was functional. Thus, the hFlex-TRAIL fusion protein may provide a novel approach, with the possible involvement of dendritic cell-mediated anti-cancer immunity, for the treatment of TRAIL-sensitive tumors.

L6 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:631148 CAPLUS
TI Spinal implant device
IN Nolan, Wesley A.
PA USA
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6117174	A	20000912	US 1998-154327	19980916
PRAI	US 1998-154327		19980916		

AB A dynamic fusion device for facilitating arthrodesis in a disc space between adjacent vertebrae that includes a body and an engaging member. The body extends along a longitudinal axis having a first portion and two or more legs depending from the first portion. The legs are laterally spaced apart from each other and define a second end of the body spaced opposite the first end. The legs define an engaging member receiving cavity. An engaging member, such as a disc, is secured to the body and received within the engaging member receiving cavity, wherein the engaging member is secured to the body only by engagement of the engaging member with the legs. During installation, the engaging member causes the legs to flex.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2000:751639 CAPLUS
DN 134:67509
TI The virtuoso of versatility: POU proteins that flex to fit
AU Phillips, Kathryn; Luisi, Ben
CS Department of Biochemistry, University of Cambridge, Cambridge, CB2 2GA, UK
SO Journal of Molecular Biology (2000), 302(5), 1023-1039
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press
DT Journal; General Review
LA English
AB A review, with 112 refs. During the evolution of eukaryotes, a new structural motif arose by the fusion of genes encoding two different types of DNA-binding domain. The family of transcription factors which contain this domain, the POU proteins, have come to play essential roles not only in the development of highly specialized tissues, such as complex neuronal systems, but also in more general cellular housekeeping. Members of the POU family recognize defined DNA sequences, and a well-studies subset have specificity for a motif known as the octamer element which is found in the promoter region of a variety of genes. The structurally bipartite POU domain has intrinsic conformational flexibility and this feature appears to confer functional diversity to the class of transcription factors. The POU domain for which we have the most structural data is from Oct-1, which binds an eight base-pair target and variants of this octamer site. The two-part DNA-binding domain partially encircles the DNA, with the sub-domains able to assume a variety of conformations, dependent on the DNA element. Crystallog. and biochem. studies have shown that the binary complex provides distinct platforms for

the recruitment of specific regulators to control transcription. The conformability of the POU domain in molding to DNA elements and co-regulators provides a mechanism for combinatorial assembly as well as allosteric mol. recognition. We review here the structure and function of the diverse POU proteins and discuss the role of the proteins' plasticity in recognition and transcriptional regulation. (c) 2000 Academic Press.
RE.CNT 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 34 BIOENG COPYRIGHT 2006 CSA on STN
AN 2004401329 BIOENG
DN 4762532
TI Grafton super(registered) Demineralized Bone Matrix: Performance Consistency, Utility, and Value
AU Russell, JL
CS 51 James Way, Eatontown, NJ 07724, USA
SO Tissue Engineering [Tissue Eng.]. Vol. 6, no. 4, pp. 435-440. Aug 2000. ISSN: 1076-3279
DT Journal
LA English
SL English
OS Medical and Pharmaceutical Biotechnology Abstracts; Calcium & Calcified Tissue Abstracts
AN 2004401329 BIOENG
AB Use of allograft is gaining increasing acceptance as an alternative to autologous bone in the management of orthopedic problems, driven by a desire to avoid the costs and morbidity associated with graft collection. Bone allograft products exist in multiple forms suitable for a full range of procedures and in some instances, with sufficient data to support formal claims for inactivation of viruses, particularly human immunodeficiency virus (HIV) and hepatitis B and C. Allogeneic demineralized bone matrix (DBM), in particular, is an appealing material because, when properly processed, it has inherent osteoinductive and osteoconductive characteristics. Allogeneic DBM often in combination with autologous bone has with few exceptions performed similarly to autologous bone in healing long bone defects created in both higher- and lower-order animals. A review of the clinical literature shows that DBM grafts have supported healing, without complication, and with a diminished need to resort to second site surgery. However, not all DBM is the same, as processing variables can contribute substantially to differences in performance. Having a biocompatible graft material that can support, if not enhance, repair, be replaced by host bone and is available in formulation options easily tailored to the procedure, represents a key goal for all bone graft substitutes. The Grafton super(registered) line of demineralized allograft bone products exist in flowable forms (gel), pliable forms that maintain dimensional integrity (flex), and moldable forms that maintain cohesiveness (putty). These forms have found significant use to fill small irregular defects, in the repair of fractures, acetabular reconstruction and as an adjunct to spinal fusion procedures. This paper emphasizes the performance consistency that can be achieved with rigorously controlled processing and outlines studies that highlight the utility and value of these products in key orthopedic indications.

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:213963 CAPLUS
DN 129:13056
TI The Schizosaccharomyces pombe mei4+ gene encodes a meiosis-specific transcription factor containing a forkhead DNA-binding domain
AU Horie, S.; Watanabe, Y.; Tanaka, K.; Nishiwaki, S.; Fujioka, H.; Abe, H.; Yamamoto, M.; Shimoda, C.
CS Department of Biology, Faculty of Science, Osaka City University, Osaka, 558, Japan
SO Molecular and Cellular Biology (1998), 18(4), 2118-2129

CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB The mei4+ gene of the fission yeast Schizosaccharomyces pombe was cloned by functional complementation. The mei4 disruptant failed to complete meiosis-I but could proliferate normally. Mei4+ was transcribed only in meiosis-proficient diploid cells after premeiotic DNA replication. The mei4+ open reading frame encodes a 57-kDa serine-rich protein comprised of 517 amino acids with a forkhead/HNF3 DNA-binding domain in the amino-terminal region. Transcription of spo6+, a gene required for sporulation, was dependent on the mei4+ function. Two copies of the GTAAAYA consensus sequence, proposed as the binding site for human forkhead proteins, were found in the promoter region of spo6+. A gel mobility shift assay demonstrated the sequence-dependent binding of the GST-Mei4 forkhead domain fusion protein to DNA fragments with one of the consensus elements. Deletion of this consensus element from the spo6 promoter abolished the transcription of spo6+ and resulted in a sporulation deficiency. One-hybrid assay of Mei4 which was fused to the Gal4 DNA-binding domain localized the transcriptional activation domain in the C-terminal 140 amino acids of Mei4. These results indicate that Mei4 functions as a meiosis-specific transcription factor of S. pombe.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 1998159224 ESBIOBASE
TI Intervertebral measurement of lumbar segmental motion with a new measuring device
AU Zhang Y.M.; Voor M.J.; Wang M.; Johnson J.R.
CS Y.M. Zhang, 82 Orchard Avenue, Barrington, RI 02806, United States. E-mail: Lijuan-Wang@Brown.edu
SO Medical Engineering and Physics, (1998), 20/2 (139-148), 32 reference(s) CODEN: MEPHEO ISSN: 1350-4533
PUI S1350453397000532
DT Journal; Article
CY United Kingdom
LA English
SL English
AB A new Intervertebral Motion Device (IMD) was developed in this study. Depending on its configuration, the IMD was used to measure motion in the sagittal, frontal, and transverse planes. Calibration results showed that the root-mean-square (RMS) error of the IMD was 0.092 mm in axial translation, 0.065 mm in shear translation, and 0.091°in rotation. Using the IMD, nine intact human lumbosacral spine specimens (L3-S1) were tested under a simulated physiological load on an MTS (Model 858 Bionix, MTS System Corporation, Minneapolis, MN). The ranges of motion (ROMs) of intact and instrumented specimens were measured in terms of angular motion (main motion) and coupled translation in the sagittal plane, frontal plane, and angular motion in the transverse plane. The results demonstrated that simulated fusion with CD instrumentation at the level of L4-L5 significantly decreased the ROMs of L4-L5 for all man and coupled motions ($P < 0.03$). The application of CD rods has less influence on the angular ROM in L/R axial rotation compared to the angular ROMs in Flex/Ext and L/R lateral bending.

L6 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
AN 1996:394755 CAPLUS
DN 125:80723
TI Minibody: a novel engineered anti-carcinoembryonic antigen antibody fragment (single-chain Fv-CH3) which exhibits rapid, high-level targeting of xenografts
AU Hu, Shi-zhen; Shively, Louise; Raubitschek, Andrew; Sherman, Mark;

Williams, Lawrence E.; Wong, Jeffrey Y. C.; Shively, John E.; Wu, Anna M.
CS Dep. Mol. Biol., City Hope Natl. Med. Cent., Duarte, CA, 91010, USA
SO Cancer Research (1996), 56(13), 3055-3061
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB A novel engineered antibody fragment (VL-VH-CH3, or "minibody") with bivalent binding to carcinoembryonic antigen (CEA) was produced by genetic fusion of a T84.66 (anti-CEA) single-chain antibody (scFv) to the human IgG1 CH3 domain. Two designs for the connecting peptide were evaluated. In the T84.66/212 LD minibody, a two-amino acid linker (generated by fusion of restriction sites) was used to join VH and CH3. In the T84.66/212 Flex minibody, the human IgG1 hinge plus an addnl. 10 residues were used as the connecting peptide. Size exclusion chromatog. of purified minibodies demonstrated that both proteins had assembled into Mr80,000 dimers as expected. Furthermore, anal. by SDS-PAGE under nonreducing conditions was consistent with disulfide bond formation in the hinge of the T84.66 Flex minibody. Purified minibodies retained high affinity for CEA (KA, 2 + 109 M-1) and demonstrated bivalent binding to antigen. Tumor targeting properties were evaluated in vivo using athymic mice bearing LS174T human colon carcinoma xenografts. 123I-labeled T84.66 minibodies demonstrated rapid, high tumor uptake, reaching 17% injected dose/g (%ID/g) for the LD minibody and 33%ID/g for the Flex minibody at 6 h following injection. Radioiodinated minibody also cleared rapidly from the circulation, yielding high tumor:blood uptake ratios: 44.5 at 24 h for the LD minibody and 64.9 at 48 h for the Flex minibody. Rapid localization by the T84.66/212 Flex minibody allowed imaging of xenografts at 4 and 19 h after administration.

L6 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:12711 CAPLUS
DN 122:33058
TI The effect of fusion level on the Demattia flex crack resistance of calcium carbonate filled plasticized poly(vinyl chloride)
AU Axtell, F. H.; Ratanapaka, J.
CS Fac. Sci., Mahidol Univ., Bangkok, 10400, Thailand
SO Plastics, Rubber and Composites Processing and Applications (1994), 21(4), 247-53
CODEN: PRPAEP; ISSN: 0959-8111
DT Journal
LA English
AB PVC compds. of a vinyl leather formulation containing various amts. of calcium carbonate filler were prepared The influences of molding time and temperature on
PVC fusion level were determined The correlation of fusion level to the behavior during Demattia flex cracking and crack growth testing was investigated. Optimum flex cracking resistance occurred at fusion levels of 53% and 63.5% for unfilled and filled compds., resp., for the same PVC formulation. The slowest crack growth rate occurred at the fusion level of 53% for both compds.. The flex cracking behavior was characteristic of the thermal softening of PVC during fatigue. On flexing, the polymer temperature rose rapidly from 27°C to 50°C and then leveled off. The presence of filler led to accelerated failure due to voiding at the polymer-filler interface and stress concentration effects. The heat build-up during flexing was not significantly different between the unfilled and filled polymer because of the lack of interfacial interaction between the filler particles and the polymer matrix.

L6 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:529865 CAPLUS
DN 117:129865

TI Hybrid hemopoietic growth factors
IN Rosen, Jonathan I.
PA Ortho Pharmaceutical Corp., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9206116	A1	19920416	WO 1991-US7053	19910926
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9187359	A1	19920428	AU 1991-87359	19910926
	EP 503050	A1	19920916	EP 1991-918221	19910926
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05502463	T2	19930428	JP 1991-517013	19910926
	ZA 9107766	A	19930329	ZA 1991-7766	19910927
	AU 9511576	A1	19950413	AU 1995-11576	19950206
PRAI	US 1990-589958	A	19900928		
	WO 1991-US7053	A	19910926		

AB Recombinant hemopoietic mols. are provided which comprise at least a portion of a 1st hemopoietic mol. having early myeloid differentiation activity and at least a portion of a 2nd hemopoietic mol. having late myeloid differentiation activity. Nucleic acids encoding the hybrid mols. are also disclosed (amino acid sequences for the fusion proteins and corresponding nucleotide sequences included). Construction of nucleic acid sequences encoding hybrids of interleukin-3 (IL-3) with erythropoietin (Epo) or with granulocyte colony-stimulating factor is described; the hybrid genes were transfected into CHO-K1 cells. Using an in vitro assay with cell line B6SUtA (a multipotential hematopoietic progenitor cell line), hybrid IL-3:Epo Short (containing IL-3, Epo, and linker sequences) was shown to have both the activities of IL-3 and Epo.

L6 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:497445 CAPLUS
DN 119:97445
TI Low-cost light-shielding laminated films
IN Akao, Mutsuo; Osanai, Hiroyuki; Kawamura, Makoto; Nakai, Koji
PA Fuji Photo Film Co., Ltd., Japan
SO Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 519251	A2	19921223	EP 1992-109104	19920529
	EP 519251	A3	19930407		
	EP 519251	B1	19970730		
	R: DE, GB				
	JP 05045803	A2	19930226	JP 1991-337200	19911219
	JP 2799796	B2	19980921		
	JP 05050568	A2	19930302	JP 1991-337194	19911219
	JP 2627591	B2	19970709		
PRAI	JP 1991-123964	A	19910528		
	JP 1991-131056	A	19910603		
	JP 1991-171615	A	19910617		
	JP 1991-337194	A	19911219		
	JP 1991-337200	A	19911219		

AB The title films, useful for packaging photosensitive materials, are produced by blocking (joining without using adhesives or heat fusion) the inner surface of deflated films in a soft state. The cut ends are joined by heat fusion and the films are free from

curling, have high tear strength, and do not sep. at lower temps. or when laminated with other flexible sheets. Thus, a double-layer inflation film comprising an outer layer (20 μm) of an ethylene-1-hexene copolymer blend with polyethylene homopolymer 15, oil furnace C black 2, a monoglycerol ester 0.2, a dimethylpolysiloxane 0.05, and 5,8-dimethyltocotrienol 0.1%, and an inner layer (30 μm) comprising an ethylene-1-butene copolymer blend with coumarone-indene resin 5, oil furnace C black 3, dimethylpolysiloxane 0.05, and 5,8-dimethyltocotrienol 0.05%, was blow molded into a tubular film. The outer layer was heated (far IR lamps), and the inner layer joined by blocking during passing the squeeze roll (nip roll), and then slitted into 3 webs of laminated films which had adhesive strength 20 g/15 mm width, tear strength of >1600 g in both longitudinal and lateral directions, a Gelbo flex test strength of >300 times, and very small curling. The manufacturing cost of these films was reduced to <1/2 of that for a conventional film produced by laminating 2 light-shielding LDPE films.

L6 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:183136 CAPLUS
DN 116:183136
TI 110 GHz ECH heating system for DIII-D
AU Callis, R.; Cary, W.; Moeller, C.; Freeman, R.; Prater, R.; Remsen, D.; Sevier, L.
CS Gen. At., San Diego, CA, 92138-5608, USA
SO AIP Conference Proceedings (1992), 244(Radio Freq. Power Plasmas), 24-7
CODEN: APCPCS; ISSN: 0094-243X
DT Journal
LA English
AB Electron cyclotron heating (ECH) has been demonstrated to be effective at heating tokamak plasmas in DIII-D and other tokamaks. Extension of these results to higher frequency and higher power in DIII-D is planned using 110 GHz outside launch X-mode at the second harmonic. A 2 MW system constructed from 4 modules, each using a Varian 0.5 MW 110 GHz gyrotron, is scheduled to be completed by May 1992; construction of a complete 0.5 MW module is complete and is in checkout. The results of the engineering test will be reported. A unique feature of this design is the use of strongly guided HE11 modes to transmit the power over the long distances required. The choice of a strongly guided HE11 mode for transmitting the ECH power was influenced by the compact waveguide, the non-critical alignment which allows waveguide flex, the ability to use mode selective directional couplers, and finally, continuous curvature bends can be used since there are no trapped modes. The waveguide is evacuated to handle the required power d. Implementation of this design required the development of mode converters to convert from the TE15,2 mode generated by the gyrotron to the desired HE11.

L6 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:216220 CAPLUS
DN 116:216220
TI Multipurpose woven cotton and cotton/polyester blends containing crosslinked polyols affixed by a low-temperature cure
AU Vigo, Tyrone L.; Hao, Ping; Bruno, Joseph S.
CS South. Reg. Res. Cent., ARS, New Orleans, LA, USA
SO Angewandte Makromolekulare Chemie (1992), 196, 1-20
CODEN: ANMCBO; ISSN: 0003-3146
DT Journal
LA English
AB Woven cotton and cotton/polyester blend fabrics of similar construction were treated with solns. of poly(ethylene glycol) (I with mol. wts. of 600, 1,000, and 1,450 g/mol) containing tetrafunctional dimethylodihydroxyethyleneurea (II) and a mixed acid catalyst. Subsequent curing of these fabrics under selected mild conditions produced fabrics containing bound and crosslinked polyols with several improved functional

properties (thermal storage and release, flex and flat abrasion resistance, soil release and hydrophilicity). These functional property improvements were due to structural aspects of the crosslinked polyol. These structural aspects were high latent heat due to energy requirement to break intra- and intermol. hydrogen bonds and the elastomeric and hydrophilic nature of the polymer in the fiber matrix. When the fabrics were cured under the mildest conditions, these enhanced functional properties were obtained without adversely affecting the softness or hand and the air permeability of these fabrics. Best results were obtained with the I (mol. weight of 1000)/II solns. for an overall balance of improved fabric properties. Relative to untreated fabrics, treated 100% cotton fabrics had the most dramatic increase in their flex life, sometimes over an order of magnitude greater than before treatment and curing.

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:681132 CAPLUS
DN 115:281132
TI Physical and mechanical properties of Courtaulds' Filmix fabric
AU Russell, John D.
CS Mater. Lab., Wright Res. Dev. Cent., Wright-Patterson Air Force Base, OH, 45433-6533, USA
SO International SAMPE Symposium and Exhibition (1991), 36(2), 1823-35
CODEN: ISSEEG; ISSN: 0891-0138
DT Journal
LA English
AB The phys. and mech. properties of carbon fiber-reinforced PEEK Filmix laminates are studied and compared with properties of laminates made from unidirectional prepreg (APC-2). Properties measured by DSC, thermomech. anal., and dynamic mech. anal. are very similar for both product forms since the matrix is PEEK in both products. The tensile and flex strength and modulus are lower for Filmix than APC-2 due to the discontinuous fibers, fiber misalignment, and poor fiber/matrix adhesion. However, Filmix has 0° 4-point shear, in-plane shear, edge delamination, and double cantilever beam properties as good as or better than the unidirectional APC-2. This is presumably due to a z-direction reinforcement from the weave of the fabric.

L6 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1990:442155 CAPLUS
DN 113:42155
TI Laminated thermoplastic films with improved gas impermeability and their uses
IN Iwanami, Teruo; Moriyama, Takamasa; Asano, Kuniyoshi
PA Nippon Synthetic Chemical Industry Co., Ltd., Japan
SO U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 115,041, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4883696	A	19891128	US 1988-273571	19881121
	JP 63218352	A2	19880912	JP 1986-261037	19861101
	JP 06045225	B4	19940615		
PRAI	JP 1986-261037	A	19861101		
	US 1987-115041	A2	19871030		

AB Plastic laminates, having excellent gas impermeability and improved flex crack resistance, drawability, and heat moldability, and useful as packaging material for foods, comprise a layer of a composition (A) of 100 parts hydrolyzed ethylene-vinyl acetate copolymer (I) and 1-100 parts thermoplastic polyester having a glass transition temperature (Tg) -50° to +25° and a heat of fusion <30 J/g; and (B) a layer of a composition consisting of ≥1 polymer selected from a

polyolefin, polystyrene, PVC, polyamide, polycarbonate, or a polyester having a Tg >30°. A laminate was prepared by coextruding a 90:10 hydrolyzed I-thermoplastic polyester (Tg -25, heat of fusion 13 J/g) blend as an internal layer, low-d. polyethylene (II) as external layer, and maleic anhydride-modified II as adhesive layer and conditioned for 10 days at 20° and 65° relative humidity to give a laminated film having adhesion 850 g/15 mm and O permeability 1.8 initially and 2.5 mL/m2-24 h after 500 flexing cycles, compared with 550, 1.5, and >2000, resp., for a similar laminate wherein the inner layer comprised hydrolyzed I only.

L6 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1987:184377 CAPLUS
DN 106:184377
TI Metal impurities in ion and electron drift directions, for different TEXTOR discharges
AU Emmoth, B.; Nagata, S.; Bergsaaker, H.; Saatherblom, H. E.; Wienhold, P.; Winter, J.; Waelbroeck, F.
CS Res. Inst. Phys., Stockholm, S-10405, Swed.
SO Journal of Nuclear Materials (1987), 145-147, 637-41
CODEN: JNUMAM; ISSN: 0022-3115
DT Journal
LA English
AB A probe system for time-resolved impurity flex measurements was used with transmitting slit apertures open in 2 or 4 directions, for the collection of impurities in ion and e drift directions, and perpendicularly (from top and from bottom). Adjustments of limiters caused changes in the connection lengths. Higher fluxes of impurities were found on the ion drift side regardless of whether the connection length was larger or smaller than on the e drift side. A flatter radial decay of impurity fluxes was found on the e drift side. The impurity fluxes became nearly equal on both the ion and e drift sides 8 cm into the scrape-off layer. From top and from bottom, the collected impurity fluxes were smaller by a factor of 100 than the fluxes measured on the ion drift side. Expts. performed in H, D and He gave similar results, but total impurity production was different.

L6 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1987:184370 CAPLUS
DN 106:184370
TI Structure of the scrape-off layer and particle fluxes in a limiter tokamak
AU Samm, U.; Bogen, P.; Claassen, H. A.; Gerhauser, H.; Hartwig, H.; Hintz, E.; Hoethker, K.; Koenen, L.; Lie, Y. T.; et al.
CS Inst. Plasmaphys., KfA Juelich G.m.b.H., Juelich, D-5170, Fed. Rep. Ger.
SO Journal of Nuclear Materials (1987), 145-147, 206-9
CODEN: JNUMAM; ISSN: 0022-3115
DT Journal
LA English
AB The determination of e d. profiles across the scrape-off layer (SOL) with neutral beam probes (Li) in combination with a variable poloidal limiter system shows that the edge densities are not axisym. The profile near the limiter inside the SOL is much steeper than that near the symmetry plane of the flux tube. This result is reproduced by a 2-D MHD model of the SOL where particle sources coming from neutrals, which are released from the limiter, are essential. By using the profile measurements, a particle flux balance can be calculated for radial diffusion, toroidal flow and recycling of neutrals which confirms the picture.

L6 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
AN 1985:486158 CAPLUS
DN 103:86158
TI Antigenic determinants of influenza virus hemagglutinin. XI. Conformational changes detected by monoclonal antibodies

AU Jackson, David C.; Nestorowicz, Ann
CS Dep. Microbiol., Univ. Melbourne, Parkville, 3052, Australia
SO Virology (1985), 145(1), 72-83
CODEN: VIRLAX; ISSN: 0042-6822
DT Journal
LA English
AB At pH 5 influenza virus hemagglutinin undergoes an irreversible conformational change which parallels the appearance of fusion activity of this mol. This conformational change was explored using a panel of monoclonal antibodies which define 4 of the major antigenic sites of this protein. Three of the major antigenic sites of hemagglutinin undergo changes when exposed to acid pH. These changes have little effect on the binding avidity of influenza virus to glycophrin, the major receptor present on the red blood cell surface. These findings were used to postulate a mechanism where the mol. flexes around a central region resulting in rearrangement in space of its component domains on exposure to low pH.

L6 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1985:96369 CAPLUS
DN 102:96369
TI Polyamide-polyoxyethylene block copolymers for production of leather substitutes
AU Yanul, N. A.; Bessonova, N. P.; Godovskii, Yu. K.; Zolotareva, A. V.; Storozhuk, I. P.; Valetskii, P. M.; Sautin, B. V.
CS Vses. Nauchno-Issled. Inst. Plenochn. Mater. Iskusstv. Kozhi, Moscow, USSR
SO Kozhevenno-Obuvnaya Promyshlennost (1984), (11), 40-2
CODEN: KOOPAJ; ISSN: 0023-4354
DT Journal
LA Russian
AB Introduction of 30% polyoxyethylene blocks into an aliphatic polyamide increased the elongation of its nonporous films from 60 to 230%, the vapor permeability from 1.36 to 2.59 mg/(cm2-h), the hygroscopicity from 7.9 to 8.9%, the flex life from 80,000 to 500,000 cycles, and the tensile strength from 29 to 31 MPa. Further increase in polyoxyethylene block concentration led to deterioration of the mech. properties of the films, though their hygienic properties continued to improve. The block copolymers comprised 2-phase systems in which crystallization and melting of one phase were influenced by those of another. The glass transition temperature, m.p., and heat of melting were determined for copolymers containing 10-90% polyoxyethylene blocks, and the heat of melting was measured for the amorphous and crystalline phases. The copolymers were used in the manufacture of leather substitutes for footwear linings.

L6 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1984:176299 CAPLUS
DN 100:176299
TI Synthesis and fiber properties of thermotropic copolyarylates containing p-benzoate as a main component
AU Jinda, Takuma; Noyori, Masaru; Matsuda, Toshikazu
CS Fiber Text. Res. Lab., Toray Ind., Inc., Sonoyama, 520, Japan
SO Sen'i Gakkaishi (1984), 40(1), T1-T6
CODEN: SENGA5; ISSN: 0037-9875
DT Journal
LA Japanese
AB Random copolyarylates containing about 80 mol% p-benzoate were prepared, using 4,4'-diacetoxybiphenyl, 3,4'-oxydibenzoic acid (I), 4,4'-oxydibenzoic acid (II), isophthalic acid (III), and/or terephthalic acid (IV) as comonomers. They formed optically anisotropic melts without thermal decomposition The enthalpies of fusion were high for the copolymers containing either I or II as the only dibasic acid component and decreased with increasing content of III or IV in the copolymers. These copolymers were melt spun

and heat treated under vacuum for several hours to yield high-strength and high-modulus fibers (tenacity 15-25 g/d, initial modulus 500-800 g/d). The tenacities of these fibers at elevated temps. were not necessarily related to the enthalpies of fusion of the copolymers and were inferior to those of Kevlar fibers; the flex fatigue endurances were higher than those of Kevlar fibers.

L6 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1981:516626 CAPLUS
DN 95:116626
TI Improvements in or relating to shoe stiffeners
IN Arnold, Brian
PA British United Shoe Machinery Co. Ltd., UK
SO Brit., 7 pp.
CODEN: BRXXAA
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 1588309	A	19810423	GB 1976-50243	19761202
PRAI	GB 1976-50243	A	19761202		

AB Compns. containing acrylonitrile-butadiene-styrene copolymer (I) [9003-56-9], nitrile rubber, PVC [9002-86-2], and plasticizer, the amts. of I, I plus PVC, I plus rubber, and rubber plus plasticizer being ≤50, <76, ≥64, and 20-30%, resp., have stiffness, resilience, lastability, flexibility, and crack resistance suitable for manufacturing stiffeners for toe and heel end parts of shoe uppers. Thus, a .apprx.0.025-in.-thick extruded sheet containing Cycolac LA 45, PVC 29.8, phthalate plasticizer 5.4, and Breon 1442 19.8 parts was coated with hot molten polyester adhesive, cooled, and shaped into a toe puff the adhesive face of which was placed over the outside of the toe end part of a shoe upper. After steam heating in a toe puff fusion press and lasting at .apprx.70° the firm toe puff was hard wearing, crack resistant, and resilient. The extruded sheet had Shore D hardness 56 and cracked after 108,000 cycles in the Satra flex test.

L6 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1970:59082 CAPLUS
DN 72:59082
TI Composite artificial ceramic tooth
IN Pettrow, John N.
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3488847	A	19700113	US 1967-624429	19670320
PRAI	US 1967-624429	A	19670320		

AB A composite artificial ceramic tooth comprises a high strength ceramic insert on the lingual surface having a preformed precise ceramic anchorage, and a feldspathic enamel-simulating portion integrally bonded by fusion t o the insert and having a molded exterior surface characterized to resemble that of a natural tooth, the insert also reinforcing the tooth to resist flexing and compression stresses. The artificial ceramic teeth comprise 2 primary portions or parts which are integrally united to form the final tooth. A typical formulation includes Al2O3 80%, SiO2 16%, H3BO3 4%. The H3BO3 acts as a flex and the inserts are fired at 2650°F for 1-2 hr. A typical formulation for the semitranslucent enamel-simulating outer portion consists of potash feldspar 70-80%, SiO2 1-20%, kaolin 1-5%, pigment and binder 1-3%. A number of different examples are described as well as a number of different

procedures and techniques for forming the insert member and anchorage.

L6 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1966:439721 CAPLUS
DN 65:39721
OREF 65:7451g-h,7452a-b
TI Manufacture of molded objects
IN Clad, Werner; Henkel, Helmut
PA Badische Anilin- & Soda-Fabrik AG
SO 3 pp.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1407446		19650730	FR 1964-987135	19640904
PRAI	DE		19630905		

AB A process to lessen the ability of absorbing H2O and of swelling of molded objects such as panels of wood chips obtained by compression of chips of wood or other large fibrous materials with binders and H2O-repellents is described. The molded object is exposed for several hours at a temperature above the fusion point of the H2O-repellent. For example, 20 g. paraffin (m. 52°) was atomized onto 3000 g. of wood chips at 110° and under a pressure of 110 atmospheric The diffusion and distribution were as fine as possible. Then, 500 g. 50% aqueous solution of a urea-formaldehyde condensate (1:18 urea-HCHO), and an aqueous solution of 4 g. of NH4Cl and 5 g. 25% NH4OH was pulverized on the wood chips in a mixer under an injection pressure of 3-5 atmospheric The mixture was preformed and the cake so formed was compressed for 7 min. at 25 kg./cm.2 at 165° to form panels 19 mm. thick. The panels were cooled with an air stream 4 days at 60 to 80°. The plaque was covered with a polyethylene foam. The flex strength was 280 kg./cm.2, the tensile strength was 8 kg./cm.2, the increase in thickness after immersion 2 hrs. in H2O was 0.5% of the dry thickness. A control panel had a flex strength of 250 kg./cm.2, a tensile strength of 8 kg./cm.2, and an increase in thickness after immersion 2 hrs. in H2O was 7.2% of the dry thickness.

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1965:447244 CAPLUS
DN 63:47244
OREF 63:8614h,8615a-b
TI Plastic coating compositions
IN Hammer, Irving P.; Taranto, Frank J.; Jakaitis, Eugene A.
PA Socony Mobil Oil Co., Inc.
SO 9 pp.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 1389415		19650219	FR 1963-927610	19630312
PRAI	US		19620312		

AB The addition of ceresin wax (I) or polyethylene (II) to coating compns. containing a paraffin wax and copolymers (III) of ethylene and vinyl acetate for use in coating cartons, such as for milk products, markedly inhibits "frosting" while retaining other desirable characteristics, such as abrasion and flex resistance, brilliance, appearance, and impermeability to vapors. Thus, a good coating was prepared from a mixture containing 50% paraffin wax (m.p. 56-57°), 20% I (m.p. 91°), and 30% III (containing 28.5% vinyl acetate, fusion index 15). Other types of coatings contain 57% petroleum wax combined with a high-mol.-weight II, or with 20% of III and II, or with 20% of a copolymer of ethylene and

Et acrylate with or without the addition of a polyterpene, which decreased the viscosity at 163°, improved the flexibility and abrasion resistance of the coating, and eliminated the small amount of frosting observed with the use of both types of copolymers. Combinations of paraffin and polypropylene with either II alone or with, e.g., 57% paraffin, 10% of a microcryst. wax m. 74°, 10% I, 9% II, and 5% polyterpene also produced good coatings depending on the end use required.

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1966:28128 CAPLUS
DN 64:28128
OREF 64:5255h,5256a-b
TI Properties of rotationally molded polyethylene
AU McKenna, L. A.
CS Union Carbide Corp., Bound Brook, NJ
SO Tech. Papers, Reg. Tech. Conf., Soc. Plastics Engrs., Akron Section (1965) 33-41
DT Journal
LA English
AB Roto-molding with polyethylene (I) powders is different from plastisol molding. The properties of I depend upon its mol. weight and crystallinity. These characteristics were measured by melt index and d. High-mol.-weight I has a low melt index. An increase in crystallinity results in an increase in d. Fusion time, low-temperature brittleness, yield strength, tear strength, and stiffness increase as the d. increases. Flex life decreases as the d. increases. Fusion time, ultimate tensile strength, and stress cracking decrease as the melt index increases. The presence of air bubbles in molded I deteriorates the ultimate phys. properties. Processing conditions, especially cooling rate and the use of mold-release agents, should be controlled for optimum polymer properties. The economics of rotational, injection, and blow molding are compared.

=> d his

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FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT 14:39:29 ON 29 JUN 2006
L1 1113 S ((FLT (N) 3) OR (FLT3) AND (CHIMERA OR CHIMAERA))
L2 78 S L1 AND FUSION
L3 6 S L1 AND FLEX
L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5 44 S (FLEX AND (FUSION OR CHIMERA OR CHIMAERA))
L6 34 DUPLICATE REMOVE L5 (10 DUPLICATES REMOVED)

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L7 5 (L6 AND TUMOR?)

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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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L8 5 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)

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L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:1082020 CAPLUS
DN 142:62606
TI Protein and nucleotide sequences and application of anti-tumor bifunctional fusion proteins
IN Ma, Jing; Guo, Yajun
PA USA
SO U.S. Pat. Appl. Publ., 158 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004254108	A1	20041216	US 2003-723003	20031126
	AU 2004252465	A1	20050106	AU 2004-252465	20040604
	CA 2528595	AA	20050106	CA 2004-2528595	20040604
	WO 2005001048	A2	20050106	WO 2004-US17765	20040604
	WO 2005001048	A3	20050616		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1633398	A2	20060315	EP 2004-776301	20040604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2005232931	A1	20051020	US 2004-4639	20041202
PRAI	CN 2003-129290	A	20030613		
	CN 2003-10119930	A	20031125		
	US 2003-723003	A	20031126		
	TW 2003-92133577	A	20031128		
	WO 2004-US17765	W	20040604		

AB Provided herein is a chimeric protein, which chimeric protein comprises a Flt3 ligand, or a biol. active fragment thereof, and a proteinuous or peptidyl tumoricidal agent, and uses thereof, particularly in the treatment of malignancy.

L8 ANSWER 2 OF 5 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-06297 BIOTECHDS
TI New CH1 deleted mimetibody polypeptide and nucleic acid, useful for diagnosing, preventing or treating cardiovascular, dermatologic, endocrine, gastrointestinal, gynecologic, infectious, neurologic and nutritional disorders;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy
AU HEAVNER G A; KNIGHT D M; GHRAYEB J; SCALLON B J; NESSPOR T C; KUTOLOSKI K A
PA CENTOCOR INC
PI WO 2004002424 8 Jan 2004
AI WO 2003-US20495 30 Jun 2003
PRAI US 2002-412144 19 Sep 2002; US 2002-392431 28 Jun 2002
DT Patent
LA English
OS WPI: 2004-082872 [08]
AN 2004-06297 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - At least one CH1 deleted mimetibody nucleic acid (I) comprises at least one polynucleotide encoding a 269 or 266 amino acid sequence

(SEQ ID NO: 1112 or 1113), given in the specification, or its complement, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) at least one CH1 deleted mimetibody nucleic acid, comprising at least one polynucleotide encoding a polypeptide with formula (I); (2) at least one CH1 deleted mimetibody polypeptide, comprising all of the contiguous amino acids of SEQ ID NO: 1112 or 1113; (3) at least one CH1 deleted mimetibody polypeptide, comprising a polypeptide with Formula (I); (4) a CH1 deleted mimetibody antibody,. comprising a monoclonal or polyclonal antibody, fusion protein, or its fragment, that specifically binds at least one CH1 deleted mimetibody polypeptide of (2) or (3); (5) a CH1 deleted mimetibody nucleic acid encoding at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody; (6) a CH1 deleted mimetibody vector comprising at least one isolated nucleic acid cited above or encoding, or complementary to such nucleic acid encoding, a CH1 deleted mimetibody polypeptide; (7) a CH1 deleted mimetibody host cell comprising an isolated nucleic acid of (6); (8) producing at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody, comprising translating a nucleic acid of (5) under conditions in vitro, in vivo or in situ, so that the CH1 deleted mimetibody or antibody is expressed in detectable or recoverable amounts; (9) a composition comprising at least one CH1 deleted mimetibody nucleic acid, CH1 deleted mimetibody polypeptide, or CH1 deleted mimetibody antibody; (10) diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal, comprising contacting or administering a composition comprising an effective amount of a composition of (9), with, or to, the cell, tissue, organ or animal; (11) a device, comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, wherein the device is suitable for contacting or administering the at least one of the CH1 deleted mimetibody polypeptide, antibody or nucleic acid, by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal; (12) an article of manufacture for human pharmaceutical or diagnostic use, comprising packaging material and a container comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (13) producing at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, comprising providing at least one host cell, transgenic animal, transgenic plant, plant cell capable of expressing in detectable or recoverable amounts the polypeptide, antibody or nucleic acid; and (14) at least one CH1 deleted mimetibody polypeptide, antibody or nucleic acid, produced by the method of (13). (V1(n)-Pep-Flex(n)-V2(n)-pHinge(n)-CH2(n)-CH3(n))(m) (I) V1 = at least one portion of an N-terminus of an immunoglobulin variable region or an Asn-terminal portion of a human variable region or Gln Ile Gln; Pep = at least one bioactive peptide from any of 42 or 609 amino acid sequences (SEQ ID NO: 1-42 or 501-1110), given in the specification; Flex = a polypeptide that provides structural flexibility by allowing the mimetibody to have alternative orientations and binding properties; V2 = at least one portion of a C-terminus of an immunoglobulin variable region or SEQ ID NO: 1126; pHinge = at least a portion of an immunoglobulin variable hinge region or SEQ ID NO: 1120; CH2 = at least a portion of an immunoglobulin CH2 constant region; CH3 = at least a portion of an immunoglobulin CH3 constant region; and n and m = an integer 1-10; In formula (I) of (3): V1 = Gln-Ile-Gln; Pep = at least one bioactive peptide selected from any of 42 amino acid sequences given in the specification (SEQ ID NOS:1-42); Flex = Gly Gly

Gly Ser; V2 = SEQ ID NO: 1126; pHinge = SEQ ID NO: 1120; CH2 = SEQ ID NO: 1121 or 1124; CH3 = SEQ ID NO:1122 or 1125; and n and m = an integer 1-10.

BIOTECHNOLOGY - Preferred Polypeptide: The polypeptide has at least one activity of at least one Pep polypeptide. Preferred Composition: The composition further comprises at least one carrier or diluent, and at least one compound, composition or polypeptide selected from at least one of a detectable label or reporter, a tumor necrosis factor (TNF) antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug, a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a form of at least one selected from a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or a powder. Preferred Method: Diagnosing or treating a CH1 deleted mimetibody ligand related condition further comprises administering, prior, concurrently or after the contacting or administering, at least one composition of at least one compound, composition or polypeptide selected from at least one of a detectable label or reporter, a TNF antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug, a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist.

ACTIVITY - Osteopathic; Cardiovascular-Gen.; Dermatological-Gen.; Auditory; Endocrine-Gen.; Gastrointestinal-Gen.; Gynecological-Gen.; Hepatotropic; Hemostatic; Immunomodulator; Antiallergic; Muscular-Gen.; Cytostatic; Antiinflammatory; Neuroleptic; Ophthalmological; Nephrotropic; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - TNF-Modulator; Cytokine-Agonist.

USE - The methods and compositions of the present invention are useful for the diagnosis, prevention and/or treatment of diseases or conditions associated with aberrant expression or activity of the CH1 deleted mimetibody, such as a bone or joint, cardiovascular, dental or oral, dermatologic, ear, nose or throat, endocrine, metabolic, gastrointestinal, gynecologic, hepatic, obstetric, hematologic, immunologic, allergic, infectious, musculoskeletal, oncologic, neurologic, nutritional, ophthalmologic, pediatric, psychiatric, renal or pulmonary disorders.

ADMINISTRATION - The effective amount of the pharmaceutical composition is 0.001-50 mg of CH1 deleted mimetibody antibody, 0.000001-500 mg of the CH1 deleted mimetibody, or 0.0001-100 microg of the CH1 deleted mimetibody nucleic acid per kilogram of the cells, tissue, organ or animal. The contacting or the administrating is by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal. (All claimed.)

EXAMPLE - Experimental protocols are described but no results given. (123 pages)

L8 ANSWER 3 OF 5 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-06296 BIOTECHDS
TI New CH1-deleted mimetibody polypeptides and nucleic acids, useful for

modulating, treating, alleviating, preventing an immune, cardiovascular, or neurodegenerative disease or disorder, anemia, cancer, or infectious diseases;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy

AU HEAVNER G A; KNIGHT D M; GHRAYEB J; SCALLON B J; NESSPOR T C; KUTOLOSKI K A

PA CENTOCOR INC

PI WO 2004002417 8 Jan 2004

AI WO 2003-US20347 27 Jun 2003

PRAI US 2002-392431 28 Jun 2002; US 2002-392431 28 Jun 2002

DT Patent

LA English

OS WPI: 2004-082870 [08]

AN 2004-06296 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A CH1-deleted mimetibody nucleic acid comprising at least one polynucleotide encoding a polypeptide having formula (I), is new.

DETAILED DESCRIPTION - A CH1-deleted mimetibody nucleic acid comprising at least one polynucleotide encoding a polypeptide having formula (I), is new. ((V1)(n)-Pep(n)-Flex(n)-V2(n)-pHinge(n)-CH2(n)-CH3(n))(m) (I). V1 = at least one portion of an N-terminus of an immunoglobulin (Ig) variable region; Pep = at least one bioactive peptide; Flex = a polypeptide that provides structural flexibility by allowing the mimetibody to have alternative orientations and binding properties; V2 = at least one portion of a C-terminus of an Ig variable region; pHinge = at least a portion of an Ig variable hinge region; CH2 = at least a portion of an Ig CH2 constant region; CH3 = at least a portion of an Ig CH3 constant region; and n and m = an integer 1-10. INDEPENDENT CLAIMS are also included for: (1) a CH1 deleted mimetibody antibody comprising a monoclonal or polyclonal antibody, fusion protein, or its fragment that specifically binds at least one CH1 deleted mimetibody polypeptide; (2) a CH1 deleted mimetibody nucleic acid encoding at least one CH1 deleted mimetibody polypeptide or the CH1 deleted mimetibody antibody;(3) a CH1 deleted mimetibody vector or host cell comprising at least one isolated nucleic acid of (2); (4) producing at least one CH1 deleted mimetibody polypeptide or CH1 deleted mimetibody antibody by translating a nucleic acid of (2) in vitro, in vivo or in situ, so that the CH1 deleted mimetibody or antibody is expressed in detectable or recoverable amounts; (5) a composition comprising at least one of the CH1 deleted mimetibody nucleic acid, polypeptide, or antibody; (6) diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal; (7) a device comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid, and suitable for contacting or administering the CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (8) an article of manufacture for human pharmaceutical or diagnostic use, comprising a packaging material and a container comprising at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid; (9) producing at least one isolated CH1 deleted mimetibody; and (10) at least one CH1 deleted mimetibody polypeptide, antibody or nucleic acid, produced from the method.

WIDER DISCLOSURE - (1) vectors comprising the CH1-deleted mimetibody nucleic acid; and (2) host cells genetically engineered with the recombinant vectors.

BIOTECHNOLOGY - Preferred Nucleic Acid: The Pep is a bioactive peptide selected from 1067 sequences (SEQ ID NOS: 43-1110) given in the specification. The CH1 deleted mimetibody polypeptide has at least one activity of at least one Pep polypeptide. Preferred Composition: The composition further comprises at least one pharmaceutical carrier or diluent, and at least one composition comprising one compound, composition or polypeptide selected from a detectable label or reporter, a tumor necrosis factor (TNF) antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an

autonomic nervous system drug, a respiratory tract drug a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or powder form. Preparation: The CH1-deleted mimetibody nucleic acid may be prepared by recombinant, synthetic or purification techniques. Preferred Method: Diagnosing or treating a CH1 deleted mimetibody ligand related condition in a cell, tissue, organ or animal, comprises contacting or administering a composition comprising at least one CH1 deleted mimetibody nucleic acid, polypeptide or antibody with or to the cell, tissue, organ or animal. The amount of CH1 deleted antibody administered is 0.001-50, 0.000001-500 mg of the CH1 deleted mimetibody, or 0.0001-100 microg of the CH1 deleted mimetibody nucleic acid per kilogram of the cells, tissue, organ or animal. Contacting or administration is by parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional; bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal means. The method further comprises administering prior, concurrently or after administration, at least one composition comprising at least one compound or polypeptide selected from a detectable label or reporter, a TNF antagonist, an anti-infective drug, a cardiovascular system drug, a central nervous system drug, an autonomic nervous system drug, a respiratory tract drug a gastrointestinal tract drug, a hormonal drug, a drug for fluid or electrolyte balance, a hematologic drug, an antineoplastic, an immunomodulation drug, an ophthalmic, otic or nasal drug, a topical drug, a nutritional drug, a cytokine, or a cytokine antagonist. The composition is in a liquid, gas, or dry, solution, mixture, suspension, emulsion or colloid, a lyophilized preparation, or powder form. Producing at least one isolated CH1 deleted mimetibody polypeptide, antibody or nucleic acid comprises providing at least one host cell, transgenic animal, transgenic plant, plant cell capable of expressing in detectable or recoverable amounts the polypeptide, antibody or nucleic acid. Preferred Article: The container is a component of a parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal delivery device or system.

ACTIVITY - Immunosuppressive; Cardiovascular; Cardiant; Hypotensive; Neuroprotective; Nootropic; Antibacterial; Virucide; Fungicide. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The CH1-deleted mimetibody is useful for diagnosing or treating a disease condition in a cell, tissue, organ or animal, specifically for modulating, treating, alleviating, preventing the incidence or reducing the symptoms of an immune, cardiovascular (e.g. arrhythmia, hypertension or heart failure), or neurodegenerative (e.g. multiple sclerosis, dementia or Alzheimer's disease) diseases or disorders, anemia, cancerous conditions, or infectious diseases (e.g. bacterial, viral or fungal infection).

ADMINISTRATION - Administration can be through parenteral, subcutaneous, intramuscular, intravenous, intraarticular, intrabronchial,

intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, intralesional, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal means (claimed) at a dose of 0.0001-500 mg/kg per single or multiple administration.

EXAMPLE - Experimental protocols are described but no results are given.(129 pages)

L8 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2001:32514653 BIOTECHNO
TI Regression of human mammary adenocarcinoma by systemic administration of a recombinant gene encoding the hFlex-TRAIL fusion protein
AU Wu X.; He Y.; Falo L.D. Jr.; Hui K.M.; Huang L.
CS Dr. L. Huang, Center for Pharmacogenetics, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15216, United States.
E-mail: Huangl@msx.upmc.edu
SO Molecular Therapy, (2001), 3/3 (368-374), 35 reference(s)
CODEN: MTOHCK ISSN: 1525-0016
DT Journal; Article
CY United States
LA English
SL English
AB The tumor necrosis factor (TNF)-related apoptosis-inducing ligand, TRAIL, is a new member of the TNF family. It can specifically induce apoptosis in a variety of human tumors. To investigate the possibility of employing the TRAIL gene for systemic cancer therapy, we constructed a recombinant gene encoding the soluble form of the human Flt3L gene (hFlex) at the 5' end and the human TRAIL gene at the 3' end. Such design allows the TRAIL gene product to be secreted into the body circulation. We have also demonstrated that the addition of an isoleucine zipper to the N-terminal of TRAIL greatly enhanced the trimerization of the fusion protein and dramatically increased its anti-tumor activity. The fusion protein reached the level of 16-38 μg/ml in the serum after a single administration of the recombinant gene by hydrodynamic-based gene delivery in mice. A high level of the fusion protein correlated with the regression of a human breast tumor established in SCID mice. No apparent toxicity was observed in the SCID mouse model. In addition, the fusion protein caused an expansion of the dendritic cell population in the C57BL/6 recipient mice, indicating that the hFlex component of the fusion protein was functional. Thus, the hFlex-TRAIL fusion protein may provide a novel approach, with the possible involvement of dendritic cell-mediated anti-cancer immunity, for the treatment of TRAIL-sensitive tumors.

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:394755 CAPLUS
DN 125:80723
TI Minibody: a novel engineered anti-carcinoembryonic antigen antibody fragment (single-chain Fv-CH3) which exhibits rapid, high-level targeting of xenografts
AU Hu, Shi-zhen; Shively, Louise; Raubitschek, Andrew; Sherman, Mark; Williams, Lawrence E.; Wong, Jeffrey Y. C.; Shively, John E.; Wu, Anna M.
CS Dep. Mol. Biol., City Hope Natl. Med. Cent., Duarte, CA, 91010, USA
SO Cancer Research (1996), 56(13), 3055-3061
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB A novel engineered antibody fragment (VL-VH-CH3, or "minibody") with

bivalent binding to carcinoembryonic antigen (CEA) was produced by genetic fusion of a T84.66 (anti-CEA) single-chain antibody (scFv) to the human IgG1 CH3 domain. Two designs for the connecting peptide were evaluated. In the T84.66/212 LD minibody, a two-amino acid linker (generated by fusion of restriction sites) was used to join VH and CH3. In the T84.66/212 Flex minibody, the human IgG1 hinge plus an addnl. 10 residues were used as the connecting peptide. Size exclusion chromatog. of purified minibodies demonstrated that both proteins had assembled into Mr80,000 dimers as expected. Furthermore, anal. by SDS-PAGE under nonreducing conditions was consistent with disulfide bond formation in the hinge of the T84.66 Flex minibody. Purified minibodies retained high affinity for CEA (KA, 2 + 109 M-1) and demonstrated bivalent binding to antigen. Tumor targeting properties were evaluated in vivo using athymic mice bearing LS174T human colon carcinoma xenografts. 123I-labeled T84.66 minibodies demonstrated rapid, high tumor uptake, reaching 17% injected dose/g (%ID/g) for the LD minibody and 33%ID/g for the Flex minibody at 6 h following injection. Radioiodinated minibody also cleared rapidly from the circulation, yielding high tumor :blood uptake ratios: 44.5 at 24 h for the LD minibody and 64.9 at 48 h for the Flex minibody. Rapid localization by the T84.66/212 Flex minibody allowed imaging of xenografts at 4 and 19 h after administration.

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     (FILE 'HOME' ENTERED AT 14:38:47 ON 29 JUN 2006)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     14:39:29 ON 29 JUN 2006
L1          1113 S ((FLT (N) 3) OR (FLT3) AND (CHIMERA OR CHIMAERA))
L2            78 S L1 AND FUSION
L3             6 S L1 AND FLEX
L4             2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5            44 S (FLEX AND (FUSION OR CHIMERA OR CHIMAERA))
L6            34 DUPLICATE REMOVE L5 (10 DUPLICATES REMOVED)
L7             5 S (L6 AND TUMOR?)
L8             5 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)

=> s l1 and tumor
L9          241 L1 AND TUMOR

=> s l9 and apoptosis
L10          25 L9 AND APOPTOSIS

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L10
L11           15 DUPLICATE REMOVE L10 (10 DUPLICATES REMOVED)

=> d l111 bib abs 1-15
L111 NOT FOUND
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d l11 bib abs 1-15

L11  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:193122  CAPLUS
DN   144:272345
TI   Gene expression profiles in white adipose tissue in the diagnosis and
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prophylaxis of hyperinsulinemia and type II diabetes
IN Kopchick, John J.; Kelder, Bruce; Boyce, Keith S.; Nagatami, Sheila
PA Ohio University, USA; Icoria, Inc.
SO PCT Int. Appl., 701 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006023121	A1	20060302	WO 2005-US23881	20050707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-591077P P 20040727
AB Mouse genes differentially expressed in comparisons of normal vs. hyperinsulinemic, hyperinsulinemic vs. type 2 diabetic, and normal vs. type 2 diabetic visceral white adipose tissue by DNA microarray hybridization have been identified, as have corresponding human genes and proteins. The human mols., or antagonists thereof, may be used for protection against hyperinsulinemia or type 2 diabetes, or their sequelae.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2005:395470 CAPLUS
DN 142:442896
TI Methods for differentiating stem cells using a self-replicating neocentromeric artificial chromosome with chromatin domains expressing transgenes for gene therapy
IN Choo, Kong-Hong Andy; Wong, Lee Hwa; Saffery, Richard Eric
PA Murdoch Childrens Research Institute, Australia
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005040391	A1	20050506	WO 2004-AU1469	20041025

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI AU 2003-905894 A 20031027
AB The present invention relates to the field of tissue engineering and genetic manipulation of cells and to methods for generating tissue suitable for use in repair, replacement, rejuvenation or augmentation

therapy. The present invention contemplates a method for genetically manipulating a stem cell by introducing a nucleic acid mol. comprising a centromere or neo-centromere into the stem cell, wherein the nucleic acid mol. conveys genetic information which is capable of introducing to or modifying a trait within the stem cell or progeny of the stem cell such as but not limited to modulating the level of stem cell proliferation, differentiation and/or self-renewal. The neo-centromere is devoid of α-satellite repeat DNA. One aspect of the present invention provides a stem cell comprising a self-replicating artificial chromosome with a neo-centromere having centromeric chromatin domains comprising expressible genetic material which modifies or introduces at least one trait in said stem cell. Microarray gene expression profiles were conducted for human 10q25 centromeric region. The engineered stem cells may also be re-programmed, for example, to direct the cells down a different cell lineage.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2005:371491 CAPLUS
DN 142:423817
TI Anti-vascular and anti-proliferation methods, therapies, and combinations employing specific tyrosine kinase inhibitors
IN Nesbit, Mark; Spada, Alfred P.; He, Wei; Myers, Michael R.
PA Gencell Sas, Fr.; Aventis Pharmaceuticals Inc.
SO PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005038465	A2	20050428	WO 2004-EP12185	20041007
	WO 2005038465	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-508859P P 20031007
OS MARPAT 142:423817
AB This invention is directed to potent inhibitors of protein tyrosine kinase such as quinoline/quinoxaline compds. alone or in synergistic combination with antiangiogenic or chemotherapeutic agents for the abrogation of mature vasculature within chemotherapeutic refractory tumors, pharmaceutical compns. comprising these compds., and to the use of these compds. for treating a patient suffering from or subject to disorders/conditions involving cell proliferation, and particularly treatment of brain cancer, ovarian cancer, pancreatic cancer prostate cancer, and human leukemias, such as chronic myelogenous leukemia, acute myelogenous leukemia or acute lymphoid leukemia.

L11 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:283363 CAPLUS
DN 142:329832
TI Combination of a vegf receptor inhibitor with a chemotherapeutic agent
IN Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul

William; Wood, Jeanette Marjorie
PA Novartis Ag, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005027972	A2	20050331	WO 2004-EP10686	20040923
	WO 2005027972	A3	20051103		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004273615	A1	20050331	AU 2004-273615	20040923
	CA 2537991	AA	20050331	CA 2004-2537991	20040923
PRAI	US 2003-505250P	P	20030923		
	WO 2004-EP10686	W	20040923		

AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with :(a) a VEGF inhibitor compound;and (b) one or more chemotherapeutic agents selected from the group consisting of : a bradykinin 1 receptor or an angiotensin II antagonist ; a cyclooxygenase inhibitor , a bisphosphonate , a heparanase inhibitor (prevents heparan sulfate degradation) , e.g. , PI-88 , a biol. response modifier, preferably a lymphokine or interferons , e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways ; an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor ; a telomerase inhibitor , e.g. , telomestatin ; a protease inhibitor, a matrix metalloproteinase inhibitor , a methionine aminopeptidase inhibitor , e.g. , bengamide or a derivative thereof , or a proteasome inhibitor , e. g. , PS-341. The patient is treated with : (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of : agents used in the treatment of hematol. malignancies or FMS-like tyrosine kinase inhibitors ; an HSP90 inhibitors ; HDAC inhibitors ; mTOR inhibitors ; somatostatin receptor antagonists ; integrin antagonists ; anti-leukemic compds. ; tumor cell damaging approaches such as ionizing radiation EDG binders ; anthranilic acid amide class of kinase inhibitors ; ribonucleotide reductase inhibitors ; S-adenosylmethionine decarboxylase inhibitors ; antibodies against VEGF or VEGFR ; photodynamic therapy ; angiostatic steroids ; implants containing corticosteroids ; AT1 receptor antagonists ; ACE inhibitors.

L11 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:313329 CAPLUS
DN 143:175

TI Raf kinase as a target for anticancer therapeutics
AU Sridhar, Srikala S.; Hedley, David; Siu, Lillian L.
CS Department of Medical Oncology and Hematology, Princess Margaret Hospital, University Health Network, Toronto, ON, Can.
SO Molecular Cancer Therapeutics (2005), 4(4), 677-685
CODEN: MCTOCF; ISSN: 1535-7163
PB American Association for Cancer Research
DT Journal; General Review
LA English
AB A review. The Ras-Raf-MEK-ERK (ERK) pathway is a logical therapeutic target because it represents a common downstream pathway for several key growth factor tyrosine kinase receptors which are often mutated or overexpressed in human cancers. Although considered mainly growth-promoting, in certain contexts, this pathway also seems to be apoptosis-suppressing. Several novel agents targeting this pathway have now been developed and are in clin. trials. One of the most interesting new agents is BAY 43-9006. Although initially developed as a Raf kinase inhibitor, it can also target several other important tyrosine kinases including VEGFR-2, Flt-3, and c-Kit, which contributes to its antiproliferative and antiangiogenic properties. To date, encouraging results were seen with BAY 43-9006, particularly in renal cell cancers which are highly vascular tumors. This review will provide an overview of the ERK signaling pathway in normal and neoplastic tissue, with a specific focus on novel therapies targeting the ERK pathway at the level of Raf kinase.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:173752 CAPLUS
DN 138:215251
TI Screening assays for identifying differentiation-inducing agents, and production of differentiated cells for cell therapy
IN West, Michael D.; Page, Raymond; Scholer, Hans; Chapman, Karen
PA Advanced Cell Technology, Inc., USA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003018760	A2	20030306	WO 2002-US26945	20020826
	WO 2003018760	A3	20030821		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2458575	AA	20030306	CA 2002-2458575	20020826
	US 2003224345	A1	20031204	US 2002-227282	20020826
	EP 1444326	A2	20040811	EP 2002-759444	20020826
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005500847	T2	20050113	JP 2003-523611	20020826
PRAI	US 2001-314316P	P	20010824		
	WO 2002-US26945	W	20020826		

AB The invention relates to assays for screening growth factors, adhesion mols., immunostimulatory mols., extracellular matrix components and other

materials, alone or in combination, simultaneously or temporally, for the ability to induce directed differentiation of pluripotent and multipotent stem cells.

L11 ANSWER 7 OF 15 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-04194 BIOTECHDS
TI Transferring a protein to a cell, useful for generating vaccines against cancer, comprises coating the cell surface with a lipidated protein, and then with a fusion protein having a first domain having affinity for the lipidated protein;
fusion protein and cell transfection for use in vaccine and gene therapy
AU TYKOCINSKI M L; ZHENG G
PA TYKOCINSKI M L; ZHENG G
PI US 2003206917 6 Nov 2003
AI US 2002-205524 25 Jul 2002
PRAI US 2002-205524 25 Jul 2002; US 2000-476828 3 Jan 2000
DT Patent
LA English
OS WPI: 2003-901036 [82]
AN 2004-04194 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Transferring a protein to a cell comprises: (a) coating the surface of the cell with a first protein, wherein said first protein is a lipidated protein; and (b) contacting the cell with a second protein, which is a fusion protein having a first domain having affinity for the lipidated protein, and a second domain capable of binding to a receptor on the cell's surface.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a method of treating a patient for an illness comprising: (a) coating the surface of several cells with a first protein, where the first protein is a lipidated protein; (b) contacting the cells with a second protein, which is a fusion protein comprised of a first domain having affinity for the first protein, and a second domain capable of binding to a receptor on the cell's surface and specific for the treatment of the illness; and (c) administering the coated cells to the patient; (2) cells made from the method above; (3) a pharmaceutical composition for treating a patient for an illness comprising cells made by the method above, in a carrier; and (4) a cell comprising a cDNA sequence encoding a membrane protein having the capacity to bind a receptor or a ligand on the surface of the cell.

BIOTECHNOLOGY - Preferred Method: The cell is a T cell, which is a CD4-positive T cell, a CD8-positive T cell, or a minor-infiltrating lymphocyte. The T cell has specificity for a tumor antigen or for a viral peptide antigen. The cell may also be selected from a lymphokine-activated killer cell, a dendritic cell, a monocyte, a B cell, a natural killer cell, a neutrophil, an eosinophil, a basophil, a mast cell, a keratinocyte, an endothelial cell, an islet cell, a fibroblast, an osteoblast, a chondrocyte, a muscle cell, a neural cell, or a stem cell consisting of a hematopoietic stem cell, a mesenchymal stem cell, or an embryonic stem cell. The second domain of the fusion protein comprises a co-stimulator domain that has the ability to activate the cell, and is selected from B7-1, B7-2, ICAM-1, ICAM-2, ICAM-3, CD48, LFA-3, CD30 ligand, CD40 ligand, heat stable antigen, B7 h, 4-1BB ligand, OX40 ligand, LIGHT, CD70 and CD24. The second domain of the fusion protein comprises a major histocompatibility complex protein complexed with a peptide antigen. The second domain of the fusion protein comprises a domain selected from CD40 ligand, TRANCE, Flt-3 ligand, GM-CSF, VEGF, and FGF. The second domain of the fusion protein may also comprise an inhibitor domain that has the ability to inhibit the cell, particularly a stem cell, where the inhibitor domain has the ability to inhibit or induce apoptosis in a T cell. The inhibitor domain is selected from Fas ligand and TRAIL. The second domain of the fusion protein also comprises a poly-histidine tag. The fusion

protein comprises a chimeric Fc fusion protein and the lipidated protein is palmitated-protein A, or chelator lipid NTA-DTDA. The method further comprises purifying the cell prior to coating the surface. There is more than one second protein that is transferred to the cell. In the transfer of protein to a cell, the first domain comprises a glycophospholipid, preferably glycosyl phosphatidylinositol. Transferring a protein to a cell of a patient comprises injecting into the patient a fusion protein comprising a first domain and a second domain, where the first domain comprises a homing element capable of attaching to the cell, and the second domain is capable of binding to a receptor on the cell's surface. The homing element is a scFv or a cytokine. In the method of treating an illness, the cells are lymphokine-activated killer cells or tumor -infiltrating lymphocytes, and are injected into a cancer patient. The method further comprises culturing the cells ex vivo prior to administration to the patient. The coating and contacting steps take place in vivo or in vitro.

ACTIVITY - Cytostatic; Virucide; Immunosuppressive.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The method is useful in the generation of cancer vaccines, artificial veto cells expression one or more co-inhibitors that can be used to delete pathogenic T cells, in the establishment of animal models, and in the study of immunological issues regarding e.g. T cell activation. The cells produced from the method are useful for treating an illness including cancer, viral infection, autoimmune disease and alloimmune disease. The cells are also useful in determining co-stimulator threshold levels.

ADMINISTRATION - Administration can be intravenous.

EXAMPLE - Recombinant protein A was derivatized with the N-hydroxylsuccinimide ester of palmitic acid. The lipid derivatized protein A was purified and referred to as pal-pro A. Daudi EL-4, JY and K562 cells were separately suspended in RPMI 1640 medium, and varying concentrations of pal-prot A were added to the cell suspension. Mixture was incubated at 4degreesC for 2 hours with constant mixing. To assess the incorporation of pal-prot A on cell surfaces, cells were washed twice in buffer, and incubated on ice for 1 hour with 100 microl/ml of FITC-human IgG diluted with the same buffer. Cells were washed twice in the buffer and analyzed on a FACStar flow cytometer. Efficient incorporation of pal-prot A was observed in all cell lines used as detected with FITC-conjugated human IgG. For the negative control, non-derivatized protein A lacked the capacity to bind to the same cells. Lipidated protein was incorporated into the cell fairly rapidly. (38 pages)

L11 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2002:219505 CAPLUS
DN 137:103518
TI Vascular endothelial growth factor (VEGF)-C signaling through FLT-4 (VEGFR-3) mediates leukemic cell proliferation, survival, and resistance to chemotherapy
AU Dias, Sergio; Choy, Margaret; Alitalo, Kari; Rafii, Shahin
CS Division of Hematology/Oncology, Weill Medical College of Comell University, New York, NY, 10021, USA
SO Blood (2002), 99(6), 2179-2184
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Similar to solid tumors, growth of leukemias may also be angiogenesis dependent. Furthermore, tyrosine kinase receptors specific to endothelial cells are expressed on certain subsets of leukemias. We have previously demonstrated the existence of a VEGF/VEGFR-2 autocrine loop on leukemic cells that supports their growth and migration. Here, we demonstrate that in response to leukemia-derived proangiogenic and proinflammatory cytokines such as basic fibroblast growth factor and IL-1,

endothelial cells release increasing amts. of another vascular endothelial growth factor (VEGF) family member, VEGF-C. In turn, interaction of VEGF-C with its receptor VEGFR-3 (FLT-4) promotes leukemia survival and proliferation. We demonstrate in 2 cell lines and 5 FLT-4+ leukemias that VEGF-C and a mutant form of the mol. that lacks the KDR-binding motif induce receptor phosphorylation, leukemia proliferation, and increased survival, as determined by increased Bcl-2/Bax ratios. Moreover, VEGF-C protected leukemic cells from the apoptotic effects of 3 chemotherapeutic agents. Because most leukemic cells release proangiogenic as well as proinflammatory cytokines, our data suggest that the generation of a novel paracrine angiogenic loop involving VEGF-C and FLT-4 may promote the survival of a subset of leukemias and protect them from chemotherapy-induced apoptosis. These results identify the VEGF-C/FLT-4 pathway as a novel therapeutic target for the treatment of subsets of acute leukemia.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:620631 CAPLUS
DN 137:306731
TI Effect of ionizing radiation on hematopoietic stem and progenitor cells: place of apoptosis and potential therapeutic interest for anti-apoptotic treatment
AU Drouet, M.; Mourcin, F.; Grenier, N.; Mayol, J. F.; Leroux, V.; Sotto, J. J.; Herodin, F.
CS Unite de Radiohematologie experimentale, Centre de Recherches du Service de Sante des Armees, La Tronche, 38702, Fr.
SO Canadian Journal of Physiology and Pharmacology (2002), 80(7), 700-709
CODEN: CJPPA3; ISSN: 0008-4212
PB National Research Council of Canada
DT Journal
LA French
AB Bone marrow aplasia observed following ionizing radiation exposure (Total Body Irradiation; gamma dose range: 2-10 Gy) is a result, in particular, of the radiation-induced (RI) apoptosis in hematopoietic stem and progenitor cells (HSPC). We have previously shown in a baboon model of mobilized peripheral blood CD34+ cell irradiation in vitro that RI apoptosis in HSPC was an early event, mostly occurring within the first 24 h, which involves the CD95 Fas pathway. Apoptosis may be significantly reduced with a combination of 4 cytokines (4F): Stem Cell Factor (SCF), FLT-3 Ligand (FL), thrombopoietin (TPO), and interleukin-3 (IL-3), each at 50 ng·mL-1 (15% survival vs. <3% untreated cells, 24 h post-irradiation at 2.5 Gy). In this study we show that addition of TNF-α (800 IU/mL) induces an increase in 4F efficacy in terms of cell survival 24 h after incubation (926% survival after 24 h irradiation exposure at 2.5 Gy) and amplification (k) of CD34+ cells after 6 days in a serum free culture medium (SFM) (kCF34+ = 4.3 and 6.3 resp. for 4F and successive 4F + TNF-α/4F treatments). In addition, the 4F combination allows culture on pre-established allogenic irradiated stromal cells in vitro at 4 Gy (kCD34+ = 4.5). Overall this study suggests (i) the potential therapeutic interest for an early administration of anti-apoptotic cytokines with or without hematopoiesis inhibitors (emergency cytokine therapy) and (ii) the feasibility in the accidentally irradiated individual, of autologous cell therapy based on ex vivo expansion in order to perform autograft of residual HSPC collected after the accident.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
AN 2001:572546 CAPLUS
DN 136:148682
TI Flt-3 and its ligand are expressed in neural

crest-derived tumors and promote survival and proliferation of their cell lines

AU Timeus, Fabio; Ricotti, Emanuela; Crescenzio, Nicoletta; Garelli, Emanuela; Doria, Alessandra; Spinelli, Monica; Ramenghi, Ugo; Basso, Giuseppe

CS Department of Pediatrics, University of Torino, Turin, Italy

SO Laboratory Investigation (2001), 81(7), 1025-1037
CODEN: LAINAW; ISSN: 0023-6837

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Flt-3 ligand (FL) is a cytokine that promotes the survival, proliferation, and differentiation of hematopoietic progenitors in synergy with other growth factors, such as stem cell factor. Previously we have demonstrated that stem cell factor and its receptor c-kit are expressed in neural crest-derived tumor cells and that a c-kit block induces their apoptosis. Here we have evaluated the expression of flt-3 and its ligand in 12 neuroectodermal tumor cell lines from neuroblastoma (NB), neuroepithelioma (NE), Ewing sarcoma (ES), and peripheral neuroectodermal tumor (PNET) and in 38 biopsies: 19 from NB and 19 from ES and PNET. RT-PCR demonstrated the expression of flt-3 and FL in all lines. Coexpression was observed in 42% of NB and in 74% of ES and PNET biopsies. Flow cytometry confirmed the presence of membrane and cytoplasmic flt-3 and membrane FL in all lines, whereas soluble FL protein was not measurable in their supernatants. Microphysiometric demonstration of acidification of the medium provided evidence of the specific response of cell lines to FL stimulation. Specific flt-3 phosphorylation after FL treatment was also demonstrated by Western blotting anal. In cells growing in RPMI plus 1% fetal calf serum, FL revealed a significant proliferating activity, more evident in NB and NE lines (mean increase of viable cells, 73 ± 26% after 1 day). Treatment with flt-3 antisense oligonucleotides significantly inhibited cell growth. FL also displayed an antiapoptotic activity: after a 12-h culture in the presence of 0.1% fetal calf serum, FL caused a 50% reduction of apoptotic cells. These results provide further evidence that neuroectodermal and hematopoietic cells share common regulatory pathways, and could be of interest in the clin. management of neuroectodermal tumors.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 15 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
DUPLICATE

AN 2000:30041656 BIOTECHNO

TI CD13/N-aminopeptidase is involved in the development of dendritic cells and macrophages from cord blood CD34.sup.+ cells

AU Rosenzwajg M.; Tailleux L.; Gluckman J.C.

CS J.C. Gluckman, Laboratoire d'Immunologie, CERVI, Hopital de la Pitie-Salpetriere, 83 Bid de l'Hopital, 75651 Paris Cedex 13, France.

SO Blood, (15 JAN 2000), 95/2 (453-460), 58 reference(s)
CODEN: BLOOAW ISSN: 0006-4971

DT Journal; Article

CY United States

LA English

SL English

AB Expression of CD13/N-aminopeptidase may reflect cell activation and growth. We examined its role regarding cell growth in cultures of cord blood CD34.sup.+ cells with stem cell factor/Flt-3 ligand/granulocyte-macrophage colony-stimulating factor/tumor necrosis factor-α indeed, 82% ± 6% of cells from culture day 5 were CD13(hi), 25% ± 8% of which were still Lin-. About 50% of CD13(hi)Lin- cells, which comprise progenitors of dendritic cells (DC), monocytes/macrophages and granulocytes, and 30% of CD13(lo)Lin- cells

were CD34.sup.+. Sorted CD34.sup.+CD13(hi)Lin- cells, cultured further for 7 days with the same cytokines, expanded 31-fold and CD34-CD13(hi)Lin- cells 7-fold, but CD34.sup.+CD13(lo)Lin- and CD34-CD13(lo)Lin- cells did not grow. Thus, cell growth correlated with CD13 expression, all the more so that cells were CD34.sup.+. Actinonin, the most potent N-aminopeptidase inhibitor, was used to engage CD13 on sorted CD13(hi)Lin- cells and on culture day-7 bulk cells. In both cases, this resulted in reversible cell growth arrest, with 30% to 60% fewer cells in the G2/S-M phase than in controls. Interestingly, similar effects were noted with CD13 monoclonal antibody TUK1, which does not inhibit N-aminopeptidase activity, but not with N-aminopeptidase-blocking antibodies WM15 and F23. All cycling cells appeared susceptible to actinonin, which induced cell apoptosis at the same time as Bcl-2 was downregulated and caspase-3 activity increased, but finally percentages and yields of DC and macrophage precursors were affected more than those of granulocytic cells. Thus, through engagement of N-aminopeptidase enzymatic site but possibly also of an independent determinant, CD13 plays a role in the growth of DC/macrophage progenitors and precursors.

L11 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:843709 CAPLUS
DN 135:117672
TI Construction and characterization of TK/FL recombinant protein
AU Wang, Xiao; Li, Liang; Feng, Kai
CS Beijing Institute of Radiation Medicine, Beijing, 100850, Peop. Rep. China
SO Zhonghua Weishengwuxue He Mianyixue Zazhi (2000), 20(5), 397-401
CODEN: ZWMZDP; ISSN: 0254-5101
PB Weishenbu Beijing Shengwu Zhipin Yanjiuso
DT Journal
LA Chinese
AB To determine the in vitro behavior of simultaneously expressed TK and FL in cells. A recombinant vector carrying herpes simplex virus thymidine kinase gene (TK), internal ribosome entry site (IRES) and Flt-3 ligand gene (FL) was constructed, and transfected into the MCF-7 tumor cells (MCF-7/TK-FL). FL in the supernatant was detected by ELISA. MTr was adopted to determine the sensitivity of MCF-7/TK-FL cells to GCV (ganciclovir). The apoptosis of cells was monitored using electro-microscope and flow cytometry. MCF-7/TK-FL cells expressed both TK and FL genes simultaneously. Dose-dependent cell killing by a transduction of the HSV-TK gene followed by GCV treatment was observed Apoptosis was also obvious in the MCF-7/TK-FL cells-GCV system. The amount of FL secreted in culture supernatant of MCF-7/TK-FL cells was 15.7ng/mL from 105 cells during 4 days, as determined by ELISA. The supernatant was able to stimulate proliferation of CD34+ cells from human cord blood. MCF-7/TK-FL cells may be used as a exptl. vaccine for tumor therapy, they are also valuable in producing large quantity of FL.

L11 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:285494 CAPLUS
DN 134:361750
TI Effects of deregulated Raf and MEK 1 expression on the cytokine-dependency of hematopoietic cells
AU McCubrey, James A.; Steelman, Linda S.; Moye, Phillip W.; Hoyle, Paul E.; Weinstein-Oppenheimer, Caroline; Chang, Fumin; Pearce, Marianne; White, Martyn K.; Franklin, Richard; Blalock, William L.
CS Department of Microbiology & Immunology, Leo Jenkins Cancer Center, East Carolina University School of Medicine, Greenville, NC, 27858, USA
SO Advances in Enzyme Regulation (2000), 40, 305-337
CODEN: AEZRA2; ISSN: 0065-2571
PB Elsevier Science Ltd.
DT Journal
LA English

AB The proliferation of many hematopoietic precursor cells is promoted by interleukin-3 (IL-3), granulocyte/macrophage-colony stimulating factor (GM-CSF), stem cell factor (SCF), flt-3 ligand (the ligand for the tyrosine kinase receptors flt-2 and flt-3), and various other cytokines. Hematopoietic cell lines have been isolated which require IL-3 or in some cases GM-CSF for proliferation, and these cytokines can also be considered as survival factors since they act to inhibit apoptosis. FDC-P1 is an IL-3/GM-CSF-dependent cell line derived from the bone marrow of normal DBA/2 mice and is representative of early hematopoietic precursor cells. FDC-P1 cells resemble cells with a colony forming granulocyte/macrophage morphol. The human IL-3/GM-CSF dependent TF-1 cell line was isolated from a patient with an erythroleukemia. In the following study, the effects of Raf and MEK expression on cytokine-dependency and signal transduction pathways were investigated to gain a better understanding of how deregulated expression of these oncoproteins can alter the growth of human and murine hematopoietic cells. Identification of pathways that interact with the Raf/MEK/MAPK pathway to abrogate cytokine-dependency, promote cellular transformation and prevent apoptosis will aid in scientists' understanding of the mechanisms responsible for malignant transformation and tumor progression.

RE.CNT 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

AN 2000:152165 CAPLUS

DN 133:72115

TI Measurement of mRNA expression for a variety of cytokines and its receptors in bone marrows of patients with myelodysplastic syndromes

AU Allampallam, Krishnan; Shetty, Vilasini; Hussaini, Seema; Mazzoran, Lucia; Zorat, Francesca; Huang, Raywin; Raza, Azra

CS Rush-Presbyterian-St. Luke's Medical Center, Rush Cancer Institute, Chicago, IL, 60612, USA

SO Anticancer Research (1999), 19(6B), 5323-5328
CODEN: ANTRD4; ISSN: 0250-7005

PB International Institute of Anticancer Research

DT Journal

LA English

AB Myelodysplastic syndromes (MDS) are a group of disorders characterized by ineffective and dysplastic hemopoiesis. Previous studies in the lab have shown extensive apoptosis and high levels of transforming growth factor (TGF-β) and tumor necrosis factor (TNF-α) in the stromal layer of MDS bone marrow. The current study focuses on the cytokines expressed in the bone marrow parenchymal cells. Bone marrow aspirate from 5 normal donors and 26 patients with myelodysplastic syndromes were examined for mRNA expression of tumor necrosis factor alpha (TNF-α), macrophage colony stimulating factor (M-CSF), Flt-3 Ligand (Flt-3L), Flt-3 receptor (Flt-3 rec), interleukin 1β (IL 1β) and interleukin 1 receptor antagonist (IL-1 ra). Comparison of 26 MDS marrows with 5 normals showed a significantly higher value for Flt -3 rec and IL 1β ($p=0.031$ and $p=0.031$) in the former, while only Flt-1β rec was considerably higher ($p=0.016$) in newly diagnosed patients. In previously diagnosed group, Flt-3 rec ($p=0.001$), TNF-α ($p=0.04$) and IL-1β ($p=0.016$) were higher than normal while there was no statistically significant difference in the newly vs. previously diagnosed MDS cases. MRNA expression of all six cytokines measured were considerably higher in MDS when compared to normal and that these levels tend to increase with disease duration. The precise source of these cytokines as well as their role in MDS pathogenesis remains to be determined, but this study confirms our previous reports that there is no dearth of cytokines in these bizarre myelosuppressive states.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
AN 1998:401295 CAPLUS
DN 129:174485
TI Special susceptibility to apoptosis of CD1a+ dendritic cell precursors differentiating from cord blood CD34+ progenitors
AU Canque, Bruno; Camus, Sandrine; Yagello, Micael; Gluckman, Jean Claude
CS Laboratoire de Biologie et Pathologie des Deficits Immunitaires and Laboratoire d'Immunologie Cellulaire de l'Ecole Pratique des Hautes Etudes, Faculte de Medecine et Hopital Pitie-Salpetriere, Paris, 75651, Fr.
SO Stem Cells (Miamisburg, Ohio) (1998), 16(3), 218-228
CODEN: STCEEJ; ISSN: 1066-5099
PB AlphaMed Press
DT Journal
LA English
AB We analyzed the effect of tumor necrosis factor (TNF)-α on the differentiation and viability of dendritic cells (DC) generated from cord blood CD34+ progenitors cultured for five days with GM-CSF, Flt-3 ligand (FL), and stem cell factor (SCF), and then with GM-CSF only [TNF(-) cultures]. Adding TNF-α from the start [TNF(+) cultures] potentiated progenitor cell proliferation and promoted early differentiation of CD1a+ DC precursors without affecting differentiation of CD14+ cells, which comprise bipotent precursors of DC and macrophages, nor of CD15+ granulocytic cells. Use of TNF-α was associated with increased cell mortality, which peaked on culture day 10 and mainly involved CD1a+ DC. Selective apoptosis of CD1a+ DC precursors was confirmed by showing that survival of day-7-sorted CD1a+CD14- cells from TNF(+) cultures was lower than that of CD1a-CD14+ cells. That similar findings were noted for sorted CD1a+CD14- cells of TNF(-) cultures, further cultured with GM-CSF without or with TNF-α, indicates that apoptosis of CD1a+ DC precursors was not induced by TNF-α. Apoptosis of CD1a+ DC precursors occurred after the cells had lost the capacity to incorporate bromodeoxyuridine. Finally, using higher GM-CSF concns. or adding interleukin 3 (IL-3) improved viability of CD1a+ cells. Other cytokines, such as IL-4 and transforming growth factor (TGF)-β1, were ineffective in this respect, though they promoted differentiation of CD1a+ DC. These results indicate that TNF-α promotes the differentiation of CD1a+ DC precursors, which display a high susceptibility to apoptosis that can be prevented by high concns. of GM-CSF or use of IL-3, without affecting the differentiation of the CD14+ DC precursors.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:38:47 ON 29 JUN 2006)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT 14:39:29 ON 29 JUN 2006

L1 1113 S ((FLT (N) 3) OR (FLT3) AND (CHIMERA OR CHIMAERA))
L2 78 S L1 AND FUSION
L3 6 S L1 AND FLEX
L4 2 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5 44 S (FLEX AND (FUSION OR CHIMERA OR CHIMAERA))
L6 34 DUPLICATE REMOVE L5 (10 DUPLICATES REMOVED)
L7 5 S (L6 AND TUMOR?)
L8 5 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)
L9 241 S L1 AND TUMOR
L10 25 S L9 AND APOPTOSIS
L11 15 DUPLICATE REMOVE L10 (10 DUPLICATES REMOVED)

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=> s (L1 and (antibody or immunoglobulin))
L12         160 (L1 AND (ANTIBODY OR IMMUNOGLOBULIN))

=> s (l12 and (tumoricidal))
L13           0 (L12 AND (TUMORICIDAL))

=> s (l12 and (tumor or cancer? or carcinoma? or neoplas?))
L14          76 (L12 AND (TUMOR OR CANCER? OR CARCINOMA? OR NEOPLAS?))

=> duplicate remove l14
DUPLICATE PREFERENCE IS 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L14
L15          63 DUPLICATE REMOVE L14 (13 DUPLICATES REMOVED)

=> s ((sm5 (n) 1) and antibody)
L16          19 ((SM5 (N) 1) AND ANTIBODY)

=> duplicate remove l16
DUPLICATE PREFERENCE IS 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L16
L17          12 DUPLICATE REMOVE L16 (7 DUPLICATES REMOVED)

=> d l17 bib abs 1-12

L17  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:290192  CAPLUS
TI   Concordant loss of melanoma differentiation antigens in synchronous and
     asynchronous melanoma metastases: implications for immunotherapy
AU   Trefzer, Uwe; Hofmann, Maja; Reinke, Susanne; Guo, Ya-Jun; Audring, Heike;
     Spagnoli, Giulio; Sterry, Wolfram
CS   Department of Dermatology and Allergy, Skin Cancer Centre,
     Charite-Universitaetsmedizin Berlin, Berlin, Germany
SO   Melanoma Research (2006), 16(2), 137-145
     CODEN: MREEEH; ISSN: 0960-8931
PB   Lippincott Williams & Wilkins
DT   Journal
LA   English
AB   Because of its known heterogeneity, the anal. of antigen expression is
     crucial prior to the initiation of antigen-specific immunotherapy for
     melanoma.  The melanoma differentiation antigens gp100, MART-1 and
     tyrosinase are involved in a common pathway of melanin synthesis.
     Peptides derived from these melanoma differentiation antigens are used in
     the immunotherapy of melanoma and antibodies recognizing these
     antigens are commonly applied to detect melanocytic lesions.  One hundred
     and ninety-one paraffin-embedded melanoma metastases from 28 patients with
     2-19 lesions (mean, 6.8) developing synchronously (n=67) or asynchronously
     (n=124) were analyzed by immunohistochem. for the expression of the
     melanoma differentiation antigens, as well as cancer/testis antigens of
     the melanoma antigen-A (MAGE-A) family (monoclonal antibodies
     77B and 57B), anti-S100 and SM5-1.  The overall
     reactivities were 81.6% (gp100), 79.5% (MART-1), 59.6% (tyrosinase), 59.1%
     (77B), 60.7% (57B), 93.2% (S100) and 91.6% (SM5-1).
     Twenty-seven lesions (14.1%) were pos. for all tumor-associated antigens, 75
     lesions (39.2%) were neg. for one antigen and 87 lesions (45.5%) were neg.
     for several tumor-associated antigens.  Coordinated loss was found for
     lesions neg. for gp100 and MART-1 (9.4%, P<0.0005), gp100 and tyrosinase
     (11.0%, P=0.009), MART-1 and tyrosinase (15.2%, P<0.0005) and gp100,
     MART-1 and tyrosinase (8.9%, P<0.0005), which is up to six times higher
     than the expected calculated loss.  This coordinated loss of melanoma
     differentiation antigens in melanoma did not include cancer testis
     antigens and S100 or SM5-1.  On average, the melanoma
     differentiation antigens stained 50-65% of cells within a lesion, and
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10-39% of synchronous clusters were heterogeneous for melanoma differentiation antigen expression. In conclusion, broader polypeptide vaccines should be used for melanoma immunotherapy.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:120682 CAPLUS
TI The monoclonal antibody SM5-1 recognizes a fibronectin variant which is widely expressed in melanoma
AU Trefzer, Uwe; Chen, Yingwen; Herberth, Gunda; Hofmann, Maja Ann; Kiecker, Felix; Guo, Yajun; Sterry, Wolfram
CS Department of Dermatology and Allergy, Skin Cancer Center, Charite - Universitaetsmedizin Berlin, Berlin, 10117, Germany
SO BMC Cancer (2006), 6, No pp. given
CODEN: BCMACL; ISSN: 1471-2407
URL: http://www.biomedcentral.com/content/pdf/1471-2407-6-8.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Background Previously we have generated the monoclonal antibody SM5-1 by using a subtractive immunization protocol of human melanoma. This antibody exhibits a high sensitivity for primary melanomas of 99% (248/250 tested) and for metastatic melanoma of 96% (146/151 tested) in paraffin embedded sections. This reactivity is superior to the one obtained by HMB-45, anti-MelanA or anti-Tyrosinase and is comparable to anti-S100. However, as compared to anti-S100, the antibody SM5-1 is highly specific for melanocytic lesions since 40 different neoplasms were found to be neg. for SM5-1 by immunohistochem. The antigen recognized by SM5-1 is unknown. Methods In order to characterize the antigen recognized by mAb SM5-1, a cDNA library was constructed from the metastatic human melanoma cell line SMMUpos in the Uni-ZAP lambda phage and screened by mAb SM5-1. The cDNA clones identified by this approach were then sequenced and subsequently analyzed. Results Sequence anal. of nine independent overlapping clones (length 3100-5600 bp) represent fibronectin cDNA including the ED-A, but not the ED-B region which are produced by alternative splicing. The 89aa splicing variant of the IIICS region was found in 8/9 clones and the 120aa splicing variant in 1/9 clones, both of which are included in the CS1 region of fibronectin being involved in melanoma cell adhesion and spreading. Conclusions The mol. recognized by SM5-1 is a melanoma associated FN variant expressed by virtually all primary and metastatic melanomas and may play an important role in melanoma formation and progression. This antibody is therefore not only of value in immunohistochem., but potentially also for diagnostic imaging and immunotherapy.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2005:523231 CAPLUS
DN 143:58513
TI Antibodies and conjugates specific to human SM5-1 tumor antigen for cancer diagnosis, prognosis and therapy
IN Ma, Jing; Guo, Yajun
PA Symbigene Acquisition Co., Inc., USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2005053604 A2 20050616 WO 2004-US17855 20040604
WO 2005053604 A3 20060209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CN 1572800 A 20050202 CN 2003-10119926 20031125
US 2005031617 A1 20050210 US 2003-722849 20031126
AU 2004294893 A1 20050616 AU 2004-294893 20040604
CA 2528182 AA 20050616 CA 2004-2528182 20040604
EP 1631238 A2 20060308 EP 2004-776307 20040604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRAI CN 2003-129123 A 20030606
CN 2003-10119926 A 20031125
US 2003-722849 A 20031126
TW 2003-92133571 A 20031128
WO 2004-US17855 W 20040604
AB The invention concerns antibodies which is specific for SM5-1 antigen expressed in melanoma, breast cancer and hepatocellular carcinoma, and polynucleotides encoding the antibodies. The invention further concerns use of such antibodies and/or polynucleotides in diagnosing and treating malignancies.

L17 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2005:1132632 CAPLUS
DN 143:420864
TI Anti-SM5-1 antigen antibodies, derivatives and antibodies for diagnosis, prognosis and treatment of melanoma, breast cancer and hepatocellular carcinoma
IN Ma, Jing; Guo, Yanjun
PA Oncomax Acquisition Corp., USA
SO U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 722,849.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005232926	A1	20051020	US 2004-4659	20041202
	CN 1572800	A	20050202	CN 2003-10119926	20031125
	US 2005031617	A1	20050210	US 2003-722849	20031126
	WO 2006060020	A1	20060608	WO 2004-US40870	20041206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI CN 2003-129123 A 20030606
CN 2003-10119926 A 20031125

US 2003-722849 A2 20031126
US 2004-4659 A 20041202
AB The invention concerns antibodies which is specific for SM5-1 antigen expressed in melanoma, breast cancer and hepatocellular carcinoma, and polynucleotides encoding the antibodies. The invention further concerns use of such antibodies and/or polynucleotides in diagnosing and treating malignancies and metastasis.

L17 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2005:122593 CAPLUS
DN 142:217390
TI Human, mouse and chimeric or humanized monoclonal antibodies specific to tumor-associated antigen SM5-1 for diagnosis, prognosis and treatment of malignancy
IN Ma, Jing; Guo, Yajun
PA USA
SO U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005031617	A1	20050210	US 2003-722849	20031126
	AU 2004294893	A1	20050616	AU 2004-294893	20040604
	CA 2528182	AA	20050616	CA 2004-2528182	20040604
	WO 2005053604	A2	20050616	WO 2004-US17855	20040604
	WO 2005053604	A3	20060209		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1631238	A2	20060308	EP 2004-776307	20040604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	US 2005232926	A1	20051020	US 2004-4659	20041202
PRAI	CN 2003-129123	A	20030606		
	CN 2003-10119926	A	20031125		
	US 2003-722849	A	20031126		
	TW 2003-92133571	A	20031128		
	WO 2004-US17855	W	20040604		

AB The invention concerns antibodies which is specific for SM5-1 antigen expressed in melanoma, breast cancer and hepatocellular carcinoma, and polynucleotides encoding the antibodies. The invention further concerns use of such antibodies and/or polynucleotides in diagnosing and treating malignancies.

L17 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1106731 CAPLUS
DN 143:362850
TI Method and monoclonal antibody composition for diagnosis of melanocytic lesions and for immunotherapy against melanoma
IN Guo, Yajun; Ma, Jing
PA Peop. Rep. China
SO U.S. Pat. Appl. Publ., 12 pp., Cont. of U.S. Ser. No. 915,746.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005227303	A1	20051013	US 2005-146518	20050606
PRAI US 1998-110516P	P	19981201		
US 1999-451353	B1	19991201		
US 2001-915746	A1	20010726		

AB This invention relates to monoclonal antibodies that recognize an antigen specific to melanocytic lesions. These antibodies are useful in methods of isolating melanoma cells and diagnosing melanocytic lesions. These antibodies are also useful for immunotherapy against melanoma. Monoclonal antibody SM5 -1 was prepared by immunizing mice with human melanoma cell lines SMMU-1 and SMMU-2 and using the splenocytes to make hybridomas. SM5-1 was used in immunohistochem. staining of tissues. The antibody stained melanoma tissues but did not stain non-melanocytic malignant tumors or most normal human tissues.

L17 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1193815 CAPLUS
DN 144:21449
TI Immune-histological investigations on primary melanomas and their metastases with SM5-1, a new monoclonal antibody
AU Reinke, Susanne
CS Germany
SO (2004) No pp., given, http://www.meind.de/search.py?28532 Avail.: Metadata on Internet Documents, Order No. 28532
From: Metadata Internet Doc. [Ger. Diss.] 2004, (D1028-4), No pp. given
DT Dissertation
LA German
AB Unavailable

L17 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1071575 CAPLUS
DN 143:345346
TI preparation and applications of a monoclonal antibody against melanoma associated antigen composition
IN Ma, Jing; Wang, Hao; Liu, Qingfa
PA Shanghai CP Guojian Pharmaceutical Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1443778	A	20030924	CN 2002-111030	20020313
PRAI CN 2002-111030		20020313		

AB A monoclonal antibody SM5-1 against melanoma specific antigen is produced from the B cell hybridoma line (ATCC No.HB-12,588). The prepared antibody is used to detect and sep. melanoma cells. SM5-1 is also used to screen melanoma specific antigen from melanoma cDNA library transfected COS-7 cells. Fusion protein and anti-melanoma drugs containing SM5-1 are also prepared

L17 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
AN 2001:217110 CAPLUS
DN 135:287197
TI SM5-1: a new monoclonal antibody which is

highly sensitive and specific for melanocytic lesions
AU Trefzer, Uwe; Rietz, Nadine; Chen, Yingwen; Audring, Heike; Herberth, Gunda; Siegel, Petra; Reinke, Susanne; Koniger, Peter; Wu, Shuguang; Ma, Jing; Liu, Yanjun; Wang, Hao; Sterry, Wolfram; Guo, Yajun
CS Department of Dermatology and Allergy, Humboldt University Berlin, Berlin, 10117, Germany
SO Archives of Dermatological Research (2000), 292(12), 583-589
CODEN: ADREDL; ISSN: 0340-3696
PB Springer-Verlag
DT Journal
LA English
AB Antibodies such as HMB-45 and anti-S100 protein have been widely used as markers of malignant melanoma despite evidence that HMB-45 has a sensitivity of only 67-93% and S100 is nonspecific for melanoma. Using a subtractive immunization protocol in a mouse model of human melanoma, we have generated several monoclonal antibodies with putative specificity for melanoma. After initial screenings, the antibody SM5-1 was chosen because of its intriguing reactivity with melanocytic tumors in both frozen and paraffin sections. The immunohistochem. staining of SM5-1 was studied in paraffin-embedded specimens of 401 melanomas (n = 401; 250 primary melanomas, 151 metastases), melanocytic nevi of the skin (n = 16), nonmelanocytic neoplasms (n = 84). The results were compared with HMB-45 and anti-S100 staining. All antibodies reacted with nevi and 97-99% with primary melanomas. Whereas both SM5-1 and anti-S100 stained 96% (146/151) of melanoma metastases, HMB-45 correctly identified only 83% (126/151). All HMB-45-neg. metastases were pos. for SM5-1. Whereas neither SM5-1 nor HMB-45 stained any of 84 specimens from 40 different nonmelanocytic neoplasms, anti-S100 was pos. in 21/84 (25%). While the staining pattern of SM5-1 was mostly homogeneous, small tumor areas in some metastases remained unstained. Staining with SM5-1 was also observed in perivascular dendritic cells, in plasma cells, some myofibroblasts and the secretion of eccrine sweat glands. Nonactivated epidermal melanocytes, keratinocytes, endothelial cells, smooth muscle cells and peripheral nerves were all neg. for SM5-1. These results suggest that SM5-1 is highly specific, as well as sensitive, for melanocytic lesions and is useful in the immunohistochem. evaluation of melanoma.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
AN 1995:543762 CAPLUS
DN 122:312508
TI Intranasal immunization with recombinant group A streptococcal M protein fragment fused to the B subunit of Escherichia coli labile toxin protects mice against systemic challenge infections
AU Dale, James B.; Chiang, Elbert C.
CS Department of Veterans Affairs Medical Center, Memphis, TN, 38104, USA
SO Journal of Infectious Diseases (1995), 171(4), 1038-41
CODEN: JIDIAQ; ISSN: 0022-1899
DT Journal
LA English
AB A fusion gene named LT-B-M5 was constructed encoding the entire B subunit of Escherichia coli labile toxin (LT-B), a 7 amino acid proline-rich linker, and 15 N-terminal amino acids of type 5 streptococcal M protein. The purified LT-B-M5 was immunogenic in rabbits and evoked antibodies against a synthetic peptide copy of the N-terminus of M5 (SM5[1-15]) and the native M5 protein and opsonic antibodies against type 5 streptococci. The hybrid protein retained the ganglioside-binding activity of LT-B and was tested in mice for its immunogenicity after local administration. Mice that were immunized intranasally with LT-B-M5 developed serum antibodies

against SM5(1-15) and were significantly protected from death after i.p. challenge infections with type 5 streptococci. The data show that protective systemic immune responses may be evoked after intranasal immunization with a fragment of M protein fused to LT-B.

L17 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:446134 CAPLUS
DN 117:46134
TI Mapping T-cell epitopes in group A streptococcal type 5 M protein
AU Robinson, John H.; Atherton, Marian C.; Goodacre, John A.; Pinkney, Michael; Weightman, Hayley; Kehoe, Michael A.
CS Med. Sch., Univ. Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK
SO Infection and Immunity (1991), 59(12), 4324-31
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Group A streptococcal cell surface M proteins elicit highly protective, serotype-specific opsonic antibodies and many serotypes also elicit host cross-reactive antibodies, which may contribute to the pathogenesis of poststreptococcal autoimmune disease. To data, studies aimed at designing safe (non-host-cross-reactive, defined-epitope) M vaccines have focused almost exclusively on antibody epitopes. Here T-cell epitopes are identified recognized by T cells from BALB/c, C57BL/6, and CBA/Ca mice immunized with purified, recombinant serotype 5 M protein (rM5). The responses of rM5-specific, major histocompatibility complex class II-restricted, T-cell clones to synthetic peptides representing most of the M5 sequence identified at least 13 distinct T-cell recognition sites, including sites recognized by ≥1 major histocompatibility complex haplotype of mice. Although none of these sites appeared to be strongly immunodominant, an N-terminal peptide, sM5[1-35], was recognized by lymph node T cells of rM5-immunized mice and by a larger proportion of rM5-specific T-cell clones than any other individual peptide. The fine specificity of these clones was mapped with subpeptides to a single site at or overlapping the sequence ELENHDL at residues 21-27, which is in close proximity to previously mapped protective antibody epitopes. Other T-cell recognition sites are distributed throughout the M protein and include several in the highly conserved C-terminal region of the mol. One of these C-terminal sites, located within residues 300-319, was recognized by a significant proportion of T-cell clones from 2 strains of mice. Helper T-cell epitopes located in the C-terminal region of M5 are likely to be widely conserved between different M serotypes and could be particularly useful in designing multivalent, defined-epitope M vaccines.

L17 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
AN 1986:440659 CAPLUS
DN 105:40659
TI Localization of protective epitopes of the amino terminus of type 5 streptococcal M protein
AU Dale, James B.; Beachey, Edwin H.
CS Cent. Health Sci., Univ. Tennessee, Memphis, TN, 38104, USA
SO Journal of Experimental Medicine (1986), 163(5), 1191-202
CODEN: JEMEAV; ISSN: 0022-1007
DT Journal
LA English
AB A set of overlapping chemical synthesized peptides representing the amino terminus of type 5 streptococcal M protein was used to localize protective, as opposed to nonprotective and tissue-crossreactive, epitopes that might be appropriate for vaccine formulations. Rabbit antisera raised against SM5(1-35) reacted in high titer with pep M5 by ELISA and opsonized type 5 streptococci. None of the antisera crossreacted with human heart tissue or myosin. Antisera against SM5(26-35) reacted with SM5(1-35) and pep M5 but failed to opsonize type 5 streptococci. Particle-phase ELISA indicated

that SM5(26-35) antibodies were directed against nonprotective determinants of pep M5 that were not exposed on the surface of viable organisms. Opsonization and ELISA inhibition assays showed that, of the SM5(1-35) antibodies that reacted with M5, all were inhibited by SM5(14-35), whereas none was inhibited by SM5(26-35), suggesting that the protective epitopes of SM5(1-35) resided between residues 14 and 26. This was confirmed by subsequent chemical synthesis of this region; SM5(14-26) totally inhibited SM5 (1-35) antibodies that reacted with pep M5 in ELISA, and completely inhibited opsonization of type 5 streptococci by SM5(1-35) antibodies. SM5(14-26) evoked high titers of type-specific, opsonic antibodies against type 5 streptococci, confirming the protective immunogenicity of this 13-residue peptide of type 5 M protein.

PALM Intranet

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